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(54) Title: LAMININ 8 AND METHODS FOR ITS USE

(57) Abstract

The present invention provides substantially purified laminin 8, methods for making recombinant laminin 8, cells that express recombinant laminin 8, and methods for using the recombinant laminin 8 to accelerate the healing of injuries to vascular tissue and tissue of mesenchymal origin, and to promote cell attachment and migration.

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LAMININ 8 AND METHODS FOR ITS USE

Cross Reference

This application claims priority to U.S. Provisional Patent Application Serial Nos. 60/131,720 filed April 30, 1999; 60/149,738 filed August 19, 1999; 60/155,945 filed September 24, 1999; and 60/182,012 filed February 11, 2000; all of which are incorporated herein by reference in their entirety.

Field of the Invention

This application relates to purified laminin 8 and methods for its use.

Background of the Invention

Basal laminae (basement membranes) are sheet-like, cell-associated extracellular matrices that play a central role in cell growth, tissue development, and tissue maintenance. They are present in virtually all tissues, and appear in the earliest stages of embryonic development.

Basal laminae are central to a variety of architectural and cell-interactive functions: (See for example, Malinda and Kleinman, Int. J. Biochem. Cell Biol. 28:957-959 (1996); Aumailley and Krieg, J. Invest. Dermatology 106:209-214 (1996))

1. They serve as architectural supports for tissues, providing adhesive substrata for cells.
2. They create perm-selective barriers between tissue compartments that impede the migration of cells and passively regulate the exchange of macromolecules. These properties are illustrated by the kidney glomerular basement membrane, which functions as an important filtration structure, creating an effective blood-tissue barrier that is not permeable to most proteins and cells.
3. Basal laminae create highly interactive surfaces that can promote cell migration and cell elongation during embryogenesis and wound repair. Following an injury, they provide a surface upon which cells regenerate to restore normal tissue function.
4. Basal laminae present information encoded in their structure to contacting cells that is important for differentiation and tissue maintenance. This information is

communicated to the cells through various receptors that include the integrins, dystroglycan, and cell surface proteoglycans. Signaling is dependent not only on the presence of matrix ligands and corresponding receptors that interact with sufficient affinities, but also on such topographical factors as ligand density in a three-dimensional matrix "landscape", and on the ability of basal lamina components to cluster receptors. Because these matrix proteins can be long-lived, basal laminae create a "surface memory" in the basal lamina for resident and transient cells.

The basal lamina is largely composed of laminin and type IV collagen heterotrimers that in turn become organized into complex polymeric structures. To date, six type IV collagen chains and at least twelve laminin subunits have been identified. These chains possess shared and unique functions and are expressed with specific temporal (developmental) and spatial (tissue-site specific) patterns.

Laminins are a family of heterotrimeric glycoproteins that reside primarily in the basal lamina. They function via binding interactions with neighboring cell receptors, and by forming laminin networks, and they are important signaling molecules that can strongly influence cellular function. Laminins are important in both maintaining cell/tissue phenotype as well as promoting cell growth and differentiation in tissue repair and development.

Laminins are large, multi-domain proteins, with a common structural organization. The laminin molecule integrates various matrix and cell interactive functions into one molecule.

The laminin molecule is comprised of an α-, β-, and γ-chain subunit joined together through a coiled-coil domain. Within this structure are identifiable domains that possess binding activity towards other laminin and basal lamina molecules, and membrane-bound receptors. Domains VI, IVb, and IVa form globular structures, and domains V, IIIb, and IIIa (which contain cysteine-rich EGF-like elements) form rod-like structures. (Kamiguchi et al., Ann. Rev. Neurosci. 21:97-125 (1998)) Domains I and II of the three chains participate in the formation of a triple-stranded coiled-coil structure (the long arm).

Table 1 shows the individual chains that each laminin type is composed of:

TABLE 1. Known laminin family members

Protein	*Chains*
Laminin-1	α1β1γ1
Laminin-2	α2β1γ1
Laminin 3	α1β2γ1
Laminin-4	α2β2γ1
Laminin-5	α3β3γ2
Laminin-6	α3β1γ1
Laminin-7	α3β2γ1
Laminin-8	α4β1γ1
Laminin-9	α4β2γ1
Laminin-10	α5β1γ1
Laminin –11	α5β2γ1
Laminin-12	α2β1γ3

Four structurally-defined family groups of laminins have been identified. The first group of five identified laminin molecules all share the β1 and γ1 chains, and vary by their α-chain composition (α1 to α5 chain). The second group of five identified laminin molecules all share the β2 and γ1 chain, and again vary by their α-chain composition. The third group of identified laminin molecules has one identified member, laminin 5, with a chain composition of α3β3γ2. The fourth group of identified laminin molecules has one identified member, laminin 12, with the newly identified γ3 chain (α2β1γ3)

Some progress has been made in elucidating the relationship between domain structure and function. (See, for example, Wewer and Engvall, Neuromusc. Disord. 6:409-418 (1996).) The overall sequence similarity among the homologous domains in different chains varies, but it is highest in domain VI (thought to play a key role in laminin polymerization), followed by domains V (possibly involved in protein-protein interactions) and III (entactin/nidogen binding; possible cell adhesion sites), and is lowest in domains I, II (both thought to be involved in intermolecular assembly, and containing possible cell adhesion sites), and G. Not all domains are present in all 3 types of chains. The globular G domain (thought to be involved in cell receptor binding) is present only in the α chains. Other domains may not be present in all chains within a certain chain type. For example, domain VI is absent from α3, α4, and γ2 chains. (Wewer and Engvall, 1996)

As a result of their large size (>600 kD) and unique structure, the laminin molecules can be resolved in the electron microscope. (Wewer and Engvall, 1996) Typically, laminins appear as cross-shaped molecules in an EM. The three short arms of the cross represent the amino terminal portions of each of the three separate laminin chains (one short arm per chain). The long arm of the cross is composed of the C-terminal parts of the three chains, which together form a coiled coil structure. (Wewer and Engvall, 1996) The long arm ends with the globular G domain.

The coiled-coil domain of the long arm is crucial for assembly of the three chains of laminin. (Yurchenco et al., Proc. Natl. Acad. Sci. 94:10189-10194 (1997)). Disulfide bonds bridge and stabilize all three chains in the most proximal region of the long arm and join the β and γ chains in the most distal region of the long arm.

A model of laminin receptor-facilitated self-assembly, based on studies conducted with cultured skeletal myotubes and Schwann cells, predicts that laminins bind to their receptors, which freely diffuse in a fluidic membrane, when ligand-free. Receptor engagement forces the laminins into a high local two-dimensional concentration, facilitating their mass-action driven assembly into ordered surface polymers. In this process, the engaged receptors are also reorganized, accompanied by cytoskeletal rearrangements. (Colognato, J. Cell Biol. 145:619-631 (1999)) This reorganization activates the receptors, causing signal transduction with the alteration of cell expression, shape and/or behavior. The evidence is that laminins must possess both cell-interacting and architecture-forming sites, which are located in different protein domains and on different subunits.

One class of laminin receptors are the integrins, which are cell surface receptors that mediate many cell-matrix and cell-cell interactions. Integrins are heterodimers, consisting of an α and a β subunit. 16 α- and 8 β-subunits are known, and at least 22 combinations of α and β subunits have been identified to date. Some integrins have only one or a few known ligands, whereas others appear to be very promiscuous. Binding to integrins is generally of low affinity, and is dependent on divalent cations. Integrins, activated through binding to their ligands, transduce signals via kinase activation cascades, such as focal adhesion and mitogen-activated kinases. Several different integrins bind different laminin isoforms more or less

specifically. (Aumailley et al., In The Laminins, Timpl and Ekblom, eds., Harwood Academic Publishers, Amsterdam. pp. 127-158 (1996))

Laminin 8, a recently identified laminin, is composed of α4, β1, and γ1 laminin chains. The laminin α4 chain is widely distributed both in adults and during development. (Iivanainen et al., J. Biol. Chem. 272:27862-27868 (1997)) In adults it is found in the basement membrane surrounding cardiac, skeletal, and smooth muscle fibers, and in lung alveolar septa. Furthermore, it is found in the endothelial basement membrane both in capillaries and larger vessels, and in the perineurial basement membrane of peripheral nerves, as well as in intersinusoidal spaces, large arteries, and smaller arterioles of bone marrow. (Frieser et al., Eur. J. Biochemistry 246:727-735 (1997); Miner et al., J. Cell Biol. 137:685-701 (1997); Geberhiwot et al., Exptl. Cell Res. 253:723-732 (1999); Gu et al., Blood 93:2533-2542 (1999); Iivanainen et al., J. Biol. Chem. 272:27862-27868 (1997))

Laminin 8 is a major laminin isoform in the vascular endothelium (Iivanainen et al., J. Biol. Chem. 272:27862-27868 (1997); Frieser et al., 1997), is expressed and adhered to by platelets (Geberhiwot et al., Exptl. Cell Res. 253:723-732 (1999)), and is the only laminin isoform synthesized in 3T3-L1 adipocytes, with its level of synthesis shown to increase upon adipose conversion of the cells. (Niimi et al., Matrix Biology 16:223-230 (1997)) Laminin 8 was further speculated to be the laminin isoform generally expressed in mesenchymal cell lineages to induce microvessels in connective tissues. (Niimi et al., 1997).

Laminin 8 has also been identified in mouse bone marrow primary cell cultures, arteriolar walls, and intersinusoidal spaces where data indicated that it is the major laminin isoform in the developing bone marrow. (Gu et al., Blood 93:2533-2542 (1999). The investigators concluded that, due to its localization in adult bone marrow adjacent to hematopoietic cells, laminin isoforms containing the α4 chain are the most likely to have biologically relevant interactions with developing hematopoietic cells. (Gu et al., 1999)

Despite the broad tissue distribution of the laminin α4 chain and laminin 8, there is not a means to prepare substantially purified laminin 8 from cell or tissue sources for research and therapeutic purposes, nor has a means for recombinant expression of laminin 8 been developed. Such research and therapeutic purposes

include, but are not limited to, methods for treating injuries to tissue of mesenchymal origin, such as bone, cartilage, tendon, and ligament, treating injuries to vascular tissue, promoting cell attachment and migration, promoting therapeutic angiogenesis and neural regeneration, ex vivo cell therapy, improving the biocompatibility of medical devices, and preparing improved cell culture devices and media.

Thus, there is a need in the art for adequate amounts of substantially purified laminin-8 for research and therapeutic purposes, and methods for making laminin 8. Such laminin 8 could be prepared either from cell lines in culture, or via recombinant DNA technology.

A preferred method of production is the use of recombinant DNA technology to engineer a human cell line of choice to produce recombinant laminin-8 ("r-laminin 8"). A recombinant-based method of laminin-8 production has several advantages over purification from human tissue or isolation from human cell lines in culture:

1. The recombinant produced protein is free of human pathogens. While this is also true for endogenous cell culture produced protein, protein derived from human tissue carries a risk for contamination by HIV, hepatitis, and other infectious agents.

2. Expression levels of the protein, and hence yields, can be improved through the use of genetically engineered genes/vectors that enhance the production of the encoded protein.

3. It is possible to engineer additional peptide sequences to the protein chain that provides a binding site for a commercially viable affinity purification procedure.

4. The method can provide for the modification of protein structure/function through the addition, substitution, elimination, and/or other modifications of protein domain structures. For example, it may be desirable to introduce an integrin binding site (e.g. RGD), switch integrin recognition sites, or engineer in a stable binding site to a synthetic substrate. Thus, the creation of expression vectors that express laminin chains generates enormous flexibility for future uses and creates a basis for creating second generation "designer" laminins.

Summary of the Invention

The present invention fulfills the need in the art for a source of substantially purified laminin 8 protein, methods for making substantially purified recombinant laminin 8 (hereinafter referred to as r-laminin 8), pharmaceutical compositions comprising laminin 8, and methods of using laminin 8 for treating injuries to tissue of mesenchymal origin, such as bone, cartilage, tendon, and ligament, treating injuries to vascular tissue, promoting cell attachment and migration, ex vivo cell therapy, improving the biocompatibility of medical devices, and preparing improved cell culture devices and media.

In one aspect, the present invention provides recombinant host cells that express laminin 8 chains and secrete r-laminin 8. In another aspect, the present invention provides substantially purified laminin 8, and methods for producing substantially purified r-laminin 8.

In a further aspect, the present invention provides pharmaceutical compositions, comprising laminin 8 together with a pharmaceutically acceptable carrier. Such pharmaceutical compositions can optionally be provided with other extracellular matrix components.

In further aspect, the present invention provides methods and kits for accelerating the healing of injuries to tissue of mesenchymal origin, such as bone, cartilage, tendon, and ligament, treating injuries to vascular tissue, and for improving the biocompatibility of grafts used for treating such injuries. In specific examples, laminin 8 or pharmaceutical compositions thereof are used to:

a. promote re-endothelialization at the site of vascular injuries;
b. improve the "take" of grafts;
c. improve the biocompatibility of medical devices;
d. treat neural injuries (neural regeneration);
e. regulate angiogenesis; and
d. promote cell attachment and migration

by providing an amount effective of r-laminin 8 for the various methods. In preferred embodiments of all of these methods, recombinant laminin 8 is used. The kits comprise an amount of laminin 8 effective for the desired effect, and instructions for the use thereof.

In a further aspect, the present invention provides improved medical devices and grafts, and methods for preparing improved medical devices and grafts, wherein the improvement comprises applying an amount effective of laminin 8 or the pharmaceutical compositions of the invention to the device or graft for the desired application.

In a further aspect, the invention provides improved cell culture devices, and methods for preparing improved cell culture devices, for the growth and maintenance of cells in culture, by providing an amount effective of laminin 8 for the attachment of cells to a cell culture device for the subsequent proliferation/differentiation/stasis of the cells.

In another aspect, the invention provides a cell culture growth supplement, comprising laminin 8. In another aspect, the invention provides an improved cell culture growth media, wherein the improvement comprises the addition of r-laminin 8.

Brief Description of the Figures

Figure 1 is a photograph of a 3-12% gradient SDS-PAGE gel. LN-1 is laminin 1/nidogen (ndg) complex with component chain identities indicated on the left; LN-8 is recombinant laminin 8. Interpretation of r-laminin 8 protein band identities are indicated based on western blotting data: $\alpha 4$ = reactivity with anti-human laminin $\alpha 4$ and also anti-FLAG monoclonal antibody (mAb); $\beta 1$ = reactivity with polyclonal anti-murine laminin $\alpha 1/\beta 1/\gamma 1$; $\gamma 1$ = reactivity with anti-human laminin $\gamma 1$ mAb; * = reactivity with both anti-laminin $\gamma 1$ mAb and anti-murine $\alpha 1/\beta 1/\gamma 1$. Both samples were run on the same gel which was subsequently silver stained.

Figure 2 is a rotary shadowed electron micrograph or r-laminin 8. Top: low magnification field showing several r-laminin 8 molecules. Bottom: Individual molecules. Each molecule has two short arms and one long arm. In some molecules, a very short (5-10 nm) rod-like stub can be seen at the junction of the arms. Arrow: G-domain can be seen as consisting of two moieties in some molecules. (Bar = 50 nm)

Figure 3 is a graph depicting a titration of cell adhesion to r-laminin 8 or laminin 1.

Figure 4 is a graph depicting HT-1080 cell adhesion to r-laminin 8 or laminin 1 coated at 10 μg/ml on 96 well plates in the presence and absence of various function-blocking integrin antibodies and other compounds.

Figure 5 is a graph depicting bovine capillary endothelial (BCE) cell adhesion to r-laminin 8 or laminin 1 coated at 10 μg/ml on 96 well plates in the presence and absence of various function-blocking integrin antibodies and other compounds.

Figure 6 is a graph depicting immortomouse brain endothelial (IBE) cell adhesion to r-laminin 8 or laminin 1 coated at 10 μg/ml on 96 well plates in the presence and absence of various function-blocking integrin antibodies and other compounds.

Figure 7 is a graph depicting integrin α6β4-transfected K562 cell adhesion to r-laminin 8 or laminin 1 coated at 10 μg/ml on 96 well plates in the presence and absence of various function-blocking integrin antibodies and other compounds.

Figure 8 is a graph depicting integrin α6-transfected K562 cell adhesion to r-laminin 8 or laminin 1 coated at 10 μg/ml on 96 well plates in the presence and absence of various function-blocking integrin antibodies and other compounds.

Detailed Description of the Preferred Embodiments

All references, patents and patent applications are hereby incorporated by reference in their entirety.

Within this application, unless otherwise stated, the techniques utilized may be found in any of several well-known references such as: *Molecular Cloning: A Laboratory Manual* (Sambrook, et al., 1989, Cold Spring Harbor Laboratory Press), *Gene Expression Technology* (Methods in Enzymology, Vol. 185, edited by D. Goeddel, 1991. Academic Press, San Diego, CA), "Guide to Protein Purification" in *Methods in Enzymology* (M.P. Deutshcer, ed., (1990) Academic Press, Inc.); *PCR Protocols: A Guide to Methods and Applications* (Innis, et al. 1990. Academic Press, San Diego, CA), *Culture of Animal Cells: A Manual of Basic Technique, 2nd Ed.* (R.I. Freshney. 1987. Liss, Inc. New York, NY), *Gene Transfer and Expression Protocols*, pp. 109-128, ed. E.J. Murray, The Humana Press Inc., Clifton, N.J.), and the Ambion 1998 Catalog (Ambion, Austin, TX).

As used herein "laminin 8" encompasses both r-laminin 8 and heterotrimeric laminin 8 from naturally occurring sources.

As used herein, the term "r-laminin 8" refers to recombinant heterotrimeric laminin 8, expressed by a cell that has been transfected with one or more expression vectors comprising at least one nucleic acid sequence encoding a laminin δ chain selected from the α4, β1 and γ1 chains, or a portion of the chains that are capable of forming a heterotrimeric laminin 8 and maintaining laminin 8 activity, or processed forms thereof. Such r-laminin 8 can thus comprise α4, β1, and γ1 sequences from a single organism, or from different organisms. Various laminin 8 chain DNA sequences are known in the art, and the use of each to prepare the r-laminin 8 of the invention is contemplated. (See, for example, Iivanainen et al., FEBS Letters 365:183-188 (1995); Frieser et al., Eur. J. Biochem. 246:727-735 (1997); Richards et al., Eur. J. Biochem. 238:813-821 (1996); Liu and Mayne, 15:433-437 (1996); Vuolteenaho et al., J. Biol. Chem. 265:15611-15616 (1990); Kallunki et al., J. Biol. Chem. 266:221-228 (1991); Sasaki et al., J. Biol. Chem. 263:16536-16544 (1988); Sasaki and Yamada, J. Biol. Chem. 262:17111-17117 (1987); Sasaki et al., Proc. Natl. Acad. Sci. 84:935-939 (1987); Pikkarainen et al., J. Biol. Chem. 262:10454-10462 (1987); all references incorporated by reference herein in their entirety).

The invention encompasses those laminin molecules wherein one or two of the chains that make up the recombinant heterotrimeric laminin 8 are encoded by endogenous laminin 8 chains. In a preferred embodiment, cells are transfected with one or more expression vectors comprising nucleic acid sequences encoding each of the α4, β1 and γ1 chains, or a portion of each of the chains that are capable of forming a heterotrimeric laminin 8 and maintaining laminin 8 activity.

In the present invention, laminin 8 is a secreted protein, which is capable of being directed to the ER, secretory vesicles, and the extracellular space as a result of a signal sequence, as well as those proteins released into the extracellular space without necessarily containing a signal sequence. If the secreted protein is released into the extracellular space, the secreted protein can undergo extracellular processing to produce a "mature" protein. Such processing event can be variable, and thus may yield different versions of the final "mature protein". The substantially purified laminin 8 of the present invention includes heterotrimers comprising both the full length and any such processed laminin 8 chains.

As used herein, the term "substantially purified" means that the laminin 8 so designated has been separated from its in vivo cellular environment.

As used herein, a laminin 8 polypeptide chain refers to a polypeptide chain according to one or more of the following:

(a) comprises a polypeptide structure selected from the group consisting of:

1. R1-R2-R3
2. R1-R2-R3(e)
3. R3
4. R3(e)
5. R1-R3
6. R1-R3(e)
7. R2-R3
8. R2-R3(e)

wherein R1 is an amino terminal methionine; R2 is a signal sequence that is capable of directing secretion of the polypeptide, wherein the signal sequence may be the natural signal sequence for the particular laminin chain, that of another secreted protein, or an artificial sequence; R3 is a secreted laminin chain selected from the α4, β1, and γ1 chains; and R3(e) is a secreted laminin chain selected from the α4, β1, and γ1 chains that further comprises an epitope tag (such as those described below), which can be placed at any position within the laminin chain amino acid sequence; and/or

(b) is encoded by a polynucleotide that is substantially similar to one or more of the disclosed laminin chain polynucleotide sequences or portions thereof (SEQ ID NOS.: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21,23, 25, or 27); and/or

(c) is encoded by a polynucleotide that hybridizes under high or low stringency conditions to the coding regions, or portions thereof, of one or more of the recombinant laminin 8 chain DNA sequences disclosed herein (SEQ ID NOS.: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27), or complementary sequences thereof; and/or

(d) has at least 70% identity to one or more of the disclosed laminin 8 polypeptide chain amino acid sequences (SEQ ID NOS.: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, or 28), preferably at least 80% identity, and most preferably at least about 90% identity.

The phrase "substantially similar" is used herein in reference to polynucleotide or polypeptide sequences having one or more conservative variations from the laminin 8 sequences disclosed herein, including but not limited to deletions, insertions, inversions, repeats, and substitutions, wherein the resulting laminin chain is functionally equivalent to those disclosed herein.

For example, conservative polynucleotide variants may contain alterations in coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, variants in which 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, including but not limited to optimizing codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as *E. coli*).

Naturally occurring conservative variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level. Alternatively, non-naturally occurring conservative variants may be produced by mutagenesis techniques or by direct synthesis.

Using known methods of protein engineering and recombinant DNA technology, conservative polynucleotide variants may be generated to improve or alter the characteristics of the expressed laminin chain polypeptides. For instance, one or more amino acids can be deleted from the N-terminus or C-terminus of the secreted protein. (See, for example, Ron et al., J. Biol. Chem. 268: 2984-2988 (1993); Dobeli et al., J. Biotechnology 7:199-216 (1988)) Ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. (See, for example, Gayleet al., J. Biol. Chem 268:22105-22111 (1993)) Furthermore, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained.

Guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie, J. U. et al., Science 247:1306-1310 (1990), wherein

the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. (Cunningham and Wells, Science 244:1081-1085 (1989).) The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly.

The "substantially similar" polypeptides of the present invention also include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitution with one or more amino acid residues having substituents groups, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), or (iv) fusion of the polypeptide with additional amino acids, such as an IgG Fc fusion region peptide, or leader or secretory sequence, or a sequence facilitating

purification. Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)

"Stringency of hybridization" is used herein to refer to conditions under which nucleic acid hybrids are stable. The invention also includes nucleic acids that hybridize under high stringency conditions (as defined herein) to all or a portion of the coding sequences of the laminin chain polynucleotides disclosed herein, or their complements. The hybridizing portion of the hybridizing nucleic acids is typically at least 50 nucleotides in length. As known to those of skill in the art, the stability of hybrids is reflected in the melting temperature (T_M) of the hybrids. T_M decreases approximately 1-1.5°C with every 1% decrease in sequence homology. In general, the stability of a hybrid is a function of sodium ion concentration and temperature. Typically, the hybridization reaction is performed under conditions of lower stringency, followed by washes of varying, but higher, stringency. Reference to hybridization stringency relates to such washing conditions. Thus, as used herein, high stringency refers to an overnight incubation at 42° C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM sodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 μg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65°C.

Also contemplated are laminin 8-encoding nucleic acid sequences that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37°C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH_2PO_4; 0.02M EDTA,

pH 7.4), 0.5% SDS, 30% formamide, 100 ug/ml salmon sperm blocking DNA; followed by washes at 50°C with 1XSSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

As used herein, "percent identity" of two amino acids or of two nucleic acids is determined using the algorithm of Karlin and Altschul (Proc. Natl. Acad. Sci. USA 87:2264-2268, 1990), modified as in Karlin and Altschul (Proc. Natl. Acad. Sci. USA 90:5873-5877, 1993). Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul et al. (J. Mol. Biol. 215:403-410, 1990). BLAST nucleotide searches are performed with the NBLAST program, score = 100, wordlength = 12, to obtain nucleotide sequences homologous to the nucleic acid molecules of the invention. BLAST protein searches are performed with the XBLAST program, score = 50, wordlength = 3, to obtain an amino acid sequence homologus to a polypeptide of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST is utilized as described in Altschul et al. (Nucleic Acids. Res. 25:3389-3402, 1997). When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) are used. See http://www.ncbi.nlm.nih.gov.

Further embodiments of the present invention include polynucleotides encoding laminin 8 chain polypeptides having at least 70% identity, preferably at least 80% identity, and most preferably at least 90% identity to one or more of the polypeptide sequences contained in SEQ ID NO:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, or fragments thereof.

As used herein, "α4 polynucleotide" refers to polynucleotides encoding an α4 laminin chain of the same name. Such polynucleotides can be characterized by one or

more of the following: (a) the nucleotides of said polynucleotide may encode an amino acid sequence substantially similar to the sequence set forth in SEQ ID NO: 2, 4, 6, 8, 10, 12 or fragments thereof; (b) polynucleotides that encode polypeptides which share at least 70% identity, preferably 80% identity, and most preferably at least 90% identity with the sequence set forth in SEQ ID NO: 2, 4, 6, 8, 10, 12, or fragments thereof; (c) the α4 polynucleotides hybridize under low or high stringency conditions to the coding sequence set forth in one or more of SEQ ID NO: 1, 3, 5, 7, 9, 11, or fragments thereof, or complementary sequences thereof; or (d) the α4 polynucleotides encode a polypeptide with a general structure selected from (1) R1-R2-R3; (2) R1-R2-R3(e); (3) R3; (4) R3(e); (5) R1-R3; (6) R1-R3(e); (7) R2-R3; and (8) R2-R3(e); wherein R1 and R2 are as described above, and R3 and R3(e) are as described above but comprise secreted α4 chain polypeptides.

As used herein, "β1 polynucleotides" refers to polynucleotides encoding a β1 laminin chain of the same name. Such polynucleotides can be characterized by one or more of the following: (a) the nucleotides of said polynucleotides may encode an amino acid sequence substantially similar to the sequence set forth in SEQ ID NO: 14, 16, 18, 20 or fragments thereof; (b) polynucleotides that encode polypeptides which share at least 70% identity, preferably at least 80%, and most preferably at least 90% identity with one or more of the sequences set forth in SEQ ID NO: 14, 16, 18, 20 or fragments thereof; (c) the β1 polynucleotides hybridize under low or high stringency conditions to the coding sequence set forth in one or more of SEQ ID NO: 13, 15, 17, 19, fragments thereof, or complementary sequences thereof; or (d) the β1 polynucleotides encode a polypeptide with a general structure selected from (1) R1-R2-R3; (2) R1-R2-R3(e); (3) R3; (4) R3(e); (5) R1-R3; (6) R1-R3(e); (7) R2-R3; and (8) R2-R3(e); wherein R1 and R2 are as described above, and R3 and R3(e) are as described above but comprise secreted β1 chain polypeptides.

As used herein, "γ1 polynucleotides" refers to polynucleotides encoding a γ1 laminin chain of the same name. Such polynucleotides can be characterized by one or more of the following: (a) the nucleotides of said polynucleotides may encode an amino acid that is substantially similar to one or more of the sequences set forth in SEQ ID NO: 22, 24, 26, 28 or fragments thereof; (b) polynucleotides that encode polypeptides which share at least 70% identity, preferably at least 80%, and most preferably at least

90% identity with at one or more of the sequences set forth in SEQ ID NO: 22, 24, 26, 28 or fragments thereof; (c) the γ1 polynucleotides hybridize under low or high stringency conditions to the coding sequence set forth in one or more of SEQ ID NO: 21, 23, 25, 27 or complementary sequences thereof; or (d) the γ1 polynucleotides encode a polypeptide with a general structure selected from (1) R1-R2-R3; (2) R1-R2-R3(e); (3) R3; (4) R3(e); (5) R1-R3; (6) R1-R3(e); (7) R2-R3; and (8) R2-R3(e); wherein R1 and R2 are as described above, and R3 and R3(e) are as described above but comprise secreted γ1 chain polypeptides.

As used herein, the term "epitope tag" refers to a polypeptide sequence that is expressed as part of a chimeric protein, where the epitope tag serves as a recognition site for binding of antibodies generated against the epitope tag, or for binding of other molecules that can be used for affinity purification of sequences containing the tag.

As used herein, the term "increased biocompatibility" refers to reduced induction of acute or chronic inflammatory response, and reduced disruption of the proper differentiation of implant-surrounding tissues for laminin 8-coated biomaterials relative to an analogous, non-coated biomaterial.

As used herein the term "graft" refers to both natural and prosthetic grafts and implants.

In one aspect, the present invention provides r-laminin 8 expressing-cells that have been transfected with an expression vector containing promoter sequences that are operatively linked to nucleic acid sequences encoding at least one polypeptide sequence comprising the α4, β1 and γ1 chains of laminin 8, or fragments thereof, wherein the transfected cells secrete heterotrimeric laminin 8 containing the recombinant laminin chain. In a preferred embodiment, the cells are systematically transfected with recombinant expression vectors containing promoter sequences that are operatively linked to nucleic acid sequences encoding polypeptide sequences comprising the α4, β1 and γ1 chains of laminin 8 After the multiple transfections, the cells express each of the recombinant laminin 8 chains, which form the heterotrimer, before r-laminin 8 secretion into the media.

In a preferred embodiment, cDNAs encoding the α4, β1 and γ1 chains, or fragments thereof, are subcloned into an expression vector. Alternatively, laminin 8 α4, β1 and/or γ1 gene sequences, including one or more introns, can be used.

Any cell capable of expressing and secreting the r-laminin 8 can be used. Preferably, eukaryotic cells are used, and most preferably mammalian cells are used, including but not limited to kidney and epithelial cell lines. In a most preferred embodiment, the mammalian cells do not express all of the laminin 8 chains endogenously. Carbohydrate and disulfide post-translational modifications are believed to be required for laminin 8 protein folding and function. This makes the use of eukaryotic cells preferable for producing functional r-laminin 8, although other systems are useful for obtaining, for example, antigens for antibody production.

"Recombinant expression vector" includes vectors that operatively link a nucleic acid coding region or gene to any promoter capable of effecting expression of the gene product. The promoter sequence used to drive expression of the individual chains or r-laminin 8 may be constitutive (driven by any of a variety of promoters, including but not limited to, CMV, SV40, RSV, actin, EF) or inducible (driven by any of a number of inducible promoters including, but not limited to, tetracycline, ecdysone, steroid-responsive). The expression vector must be replicable in the host organisms either as an episome or by integration into host chromosomal DNA. In a preferred embodiment, the expression vector comprises a plasmid. However, the invention is intended to include other expression vectors that serve equivalent functions, such as viruses.

In one embodiment, at least one of the laminin chain polypeptide sequences, or fragments thereof, is operatively linked to a nucleic acid sequence encoding an "epitope tag", so that at least one of the chains is expressed as a fusion protein with an expressed epitope tag. The epitope tag may be expressed as the amino terminus, the carboxy terminus, or internal to any of the polypeptide chains comprising r-laminin 8, so long as the resulting r-laminin 8 remains functional. Any epitope tag may be utilized, so long as it can be used as the basis for affinity purification of the resulting r-laminin 8. Examples of such epitope tags include, but are not limited to FLAG (Sigma Chemical, St. Louis, MO), myc (9E10) (Invitrogen, Carlsbad, CA), 6-His (Invitrogen; Novagen, Madison, WI), and HA (Boehringer Manheim Biochemicals).

In another embodiment, one of the r-laminin 8 chains is expressed as a fusion protein with a first epitope tag, and at least one other r-laminin chain is expressed as a fusion protein with a second epitope tag. This permits multiple rounds of purification

to be carried out. Alternatively, the same epitope tag can be used to create fusion proteins with more than one of the r-laminin chains.

In a further embodiment, the epitope tag can be engineered to be cleavable from the r-laminin 8 chain(s). Alternatively, no epitope tag is fused to any of the r-laminin 8 chains, and the r-laminin 8 is purified by standard techniques, including but not limited to affinity chromatography using laminin 8 specific antibodies or other laminin 8 binding molecules.

Transfection of the expression vectors into eukaryotic cells can be accomplished via any technique known in the art, including but not limited to calcium phosphate co-precipitation, electroporation, or liposome mediated-, DEAE dextran mediated-, polycationic mediated-, or viral mediated transfection. Transfection of bacterial cells can be done by standard methods.

In a preferred embodiment, the cells are stably transfected. Methods for stable transfection and selection of appropriate transfected cells are known in the art. In a most preferred embodiment, a CMV promoter driven expression vector is used in a human kidney embryonic 293 cell line.

Media from cells transfected with a single laminin chain are initially analyzed on Western blots using laminin chain-specific antibodies. The expression of single laminin chains following transfection is generally intracellular. Clones showing reactivity against individual transfected chain(s) are verified by any appropriate method, such as PCR, reverse transcription-PCR, or nucleic acid hybridization, to confirm incorporation of the transfected gene. Preferably, analysis of genomic DNA preparations from such clones is done by PCR using laminin chain-specific primer pairs. Media from transfected clones producing all three chains are further analyzed for r-laminin 8 secretion and/or activity, by any appropriate method, including Western blot analysis and cell binding assays. Activity of the r-laminin 8 is preferably analyzed in a cell adhesion assay.

In another aspect, the present invention provides substantially purified laminin 8, preferably r-laminin 8. In one embodiment, the substantially purified laminin 8 comprises a first chain comprising an $\alpha 4$ chain polypeptide; a second chain comprising a $\beta 1$ chain polypeptide; and a third chain comprising a $\gamma 1$ chain polypeptide. Alternatively, the r-laminin 8 comprises a first chain that is substantially similar to at

least one of the sequences shown in SEQ ID NO: 2, 4, 6, 8, 10, 12 or fragments thereof; a second chain that is substantially similar to at least one of the sequence shown in SEQ ID NO: 14, 16, 18, 20 or fragments thereof; and a third chain that is substantially similar to the sequence shown in SEQ ID NO: 22, 24, 26, 28 or fragments thereof.

In another embodiment, the substantially purified r-laminin 8 comprises a first chain comprising a polypeptide that is at least about 70% identical to at least one of the sequences shown in SEQ ID NO: 2, 4, 6, 8, 10, 12 or fragments thereof; a second chain comprising a polypeptide that is at least 70% identical to at least one of the sequences shown in SEQ ID NO: 14, 16, 18, 20 or fragments thereof; and a third chain comprising a polypeptide that is at least 70% identical to at least one of the sequences shown in SEQ ID NO: 22, 24, 26, 28 or fragments thereof, wherein the first, second, and third polypeptides are produced recombinantly, and wherein the first, second, and third chains assemble into a recombinant heterotrimeric laminin 8.

In a preferred embodiment, at least one of the first, second, or third chains of the substantially purified human r-laminin 8 is expressed as a fusion protein with an epitope tag.

Alternatively, the r-laminin 8 comprises a heterotrimeric polypeptide structure, wherein each individual chain comprises a general structure selected from the group consisting of: (1) R1-R2-R3; (2) R1-R2-R3(e); (3) R3; (4) R3(e); (5) R1-R3; (6) R1-R3(e); (7) R2-R3; and (8) R2-R3(e)

wherein R1 is a amino terminal methionine; R2 is a signal sequence that is capable of directing secretion of the polypeptide, wherein the signal sequence may be the natural signal sequence for the particular laminin chain, that of another secreted protein, or an artificial sequence; R3 is a secreted $\alpha 4$, $\beta 1$, or $\gamma 1$ laminin chain; and R3(e) is a secreted laminin $\alpha 4$, $\beta 1$, and $\gamma 1$ chain that further comprises an epitope tag (such as those described above), which can be placed at any position within the laminin chain amino acid sequence.

In a preferred embodiment, purification of r-laminin 8 is accomplished by passing media from the transfected cells through an antibody affinity column. In one embodiment, antibodies against a peptide epitope expressed on at least one of the recombinant chains are attached to an affinity column, and bind the r-laminin 8 that has been secreted into the media. The r-laminin 8 is removed from the column by passing

excess peptide over the column. Eluted fractions are analyzed by any appropriate method, including gel electrophoresis and Western blot analysis. In a further embodiment, the peptide epitope can be cleaved after purification. In other embodiments, two or three separate r-laminin chains are expressed as fusion proteins, each with a different epitope tag, permitting two or three rounds of purification and a doubly or triply purified r-laminin 8. The epitope tag can be engineered so as to be cleavable from the r-laminin 8 chain(s) after purification. Alternatively, no epitope tag is fused to any of the r-laminin 8 chains, and the r-laminin 8 is purified by standard techniques, including but not limited to affinity chromatography using laminin 8 specific antibodies or other laminin 8 binding molecules.

The present invention further provides pharmaceutical compositions comprising substantially purified laminin 8 and a pharmaceutically acceptable carrier. In a preferred embodiment, the pharmaceutical composition comprises substantially purified r-laminin 8. According to this aspect of the invention, other agents can be included in the pharmaceutical compositions, depending on the condition being treated. The pharmaceutical composition may further comprise one or more other compounds, including but not limited to any of the collagens, other laminin types, fibronectin, vitronectin, cadherins, integrins, α-dystroglycan, entactin/nidogen, α-dystroglycan, glycoproteins, proteoglycans, heparan sulfate proteoglycan, glycosaminoglycans, epidermal growth factor, vascular endothelial growth factor, fibroblast growth factor, or nerve growth factors, and peptide fragments thereof.

Pharmaceutical preparations comprising substantially purified laminin 8 can be prepared in any suitable form, and generally comprise the laminin 8 in combination with any of the well known pharmaceutically acceptable carriers. The carriers can be injectable carriers, topical carriers, transdermal carriers, and the like. The preparation may advantageously be in a form for topical administration, such as an ointment, gel, cream, spray, dispersion, suspension or paste. The preparations may further advantageously include preservatives, antibacterials, antifungals, antioxidants, osmotic agents, and similar materials in composition and quantity as is conventional. Suitable solutions for use in accordance with the invention are sterile, are not harmful for the proposed application, and may be subjected to conventional pharmaceutical operations such as sterilization and/or may contain conventional adjuvants, such as preservatives,

stabilizers, wetting agents, emulsifiers, buffers etc. For assistance in formulating the compositions of the present invention, one may refer to Remington's Pharmaceutical Sciences, 15th Ed., Mack Publishing Co., Easton, Pa. (1975).

In further aspect, the present invention provides methods and kits comprising laminin 8, or pharmaceutical compositions thereof (and instructions for using the laminin 8 in the kits) for accelerating the healing of injuries to tissue of mesenchymal origin, such as bone, cartilage, tendon, and ligament, treating injuries to vascular and neural tissue, and for improving the biocompatibility of grafts used for treating such injuries. In a preferred embodiment of each of the methods disclosed below, r-laminin 8 is used. In specific examples, substantially purified laminin 8, r-laminin 8, or pharmaceutical compositions thereof are used to:

a. promote re-endothelialization at the site of vascular injuries;
b. improve the "take" of grafts;
c. improve the biocompatibility of medical devices;
d. treat neural injuries (neural regeneration);
e. regulate angiogenesis; and
d. promote cell attachment and migration

by providing an amount effective of laminin 8 or pharmaceutical compositions thereof for the various methods.

In one embodiment, laminin 8 is used to promote re-endothelialization, and to thus inhibit abnormal smooth muscle cell proliferation, at the site of a vascular injury. The $\alpha 4$ chain is associated with mesenchymally derived cell populations, including but not limited to endothelium and smooth muscle cells, and laminin 8 has been shown to be a primary laminin of the vascular endothelium.

The value of angioplasty in clearing occluded coronary arteries is limited by a restenosis/reocclusion rate of 50-70%. Several studies have indicated that the insertion of a vascular stent following angioplasty appears to decrease the occurrence of restenosis, but the problem still limits the effectiveness of this treatment. Restenosis appears to arise in part from the proliferation of vascular smooth muscle cells in response to the angioplasty treatment. It is likely that the scraping action of angioplasty removes not only the problematic occlusion, but also sections of the vascular basal lamina. The discontinuous basal lamina that results could contribute to

what appears to be abnormal growth of the vascular smooth muscle cells that leads to restenosis.

The attachment of laminin 8 to vascular stents can be used to limit restenosis, by promoting re-endothelialization. The interaction of vascular endothelial cells with the laminin 8 coated stents promotes their adhesion and attachment, thereby leading to homeostasis and a normal cell growth response, instead of the injury/activation endothelial cell response seen with restenosis. While activated platelets adhere to laminin 8, non-activated platelets do not. Furthermore, is has been shown that soluble laminin 8 does not cause platelet activation, but has an inhibitory effect on platelet activation by classical activators such as thrombin, collagen I, and ADP (unpublished observations). A more normal and controlled rate of re-endothelialization will decrease the incidence of re-occlusions, and improve the outcome of the angioplasty procedure.

Similarly, synthetic vascular grafts can induce blood clotting and thrombosis through interactions of blood clotting factors with the synthetic graft material. Coating vascular grafts with laminin 8 promotes endothelialization of the synthetic vessel, thereby providing for a non-thrombogenic surface. Vascular endothelial cells, like other cells that sit upon a basement membrane, prefer to adhere to an appropriate basement membrane substrate. Laminin-8 has been identified as a component of the vascular basal lamina, and is suspected to be involved in the attachment of vascular endothelial cells to the supporting basal lamina. Providing this substrate in a graft material creates a non-thrombogenic surface, promotes endothelialization, and inhibits intravascular thrombosis and vascular obstruction.

Administration to the injured blood vessel can be accomplished in some cases by simply coating laminin 8 or pharmaceutical compositions thereof into an injured area. In other embodiments, delivery can be accomplished by:

1. Coating a stent;
2. Coating a biodegradable sleeve over the stent; or
3. Forcing a liquid preparation of the laminin 8 or pharmaceutical compositions thereof through a porous catheter to the injured site.

In another embodiment, the present invention provides methods to promote bone and connective tissue repair in a subject. The incorporation of laminin 8 or pharmaceutical compositions thereof into wound repair dressings and matrices as well

as tissue grafts to accelerate the healing of bone and connective tissue repair provides a natural ligand interactive surface to promote normal cell adherence, cell growth and tissue development. Many grafts are used to replace connective tissue that has a cell layer adherent to a basal lamina. When an inappropriate surface is provided to these cells following grafting, the graft is at risk for failure of restoration of the normal cell layer. The advantage of coating these grafts with laminin 8 is to create a surface that sufficiently recapitulates a normal basal lamina surface to promote cell re-population. As used herein the term "graft" refers to both natural and prosthetic grafts.

The methods of the present invention have application in the healing of tendon, cartilage, or ligament tears, deformities and defects, bone fractures, defects, as well as use in the improved fixation of tendon, cartilage, or ligament to bone or other tissues. In addition, bony in-growth into various prosthetic devices can be greatly enhanced so that such artificial parts are firmly and permanently anchored into the surrounding skeletal tissue through a natural osseous bridge.

In a further aspect, the present invention comprises medical devices with improved biocompatibility, wherein the devices are coated with laminin 8 or pharmaceutical compositions thereof, alone or in combination with other proteins or agents that serve to increase the biocompatibility of the device surface. The coated device stimulates cell attachment and provides for diminished inflammation and/or infection at the site of entry of the appliance.

Such medical devices can be of any material used for implantation into the body, and preferably are made of or coated with a biocompatible metal that may be either stainless steel or titanium. Alternatively, the device is made of or coated with a ceramic material, or a polymer including but not limited to polyester, polyglycolic acid or a polygalactose-polyglycolic acid copolymer.

One particular use of the present invention is to increase cell adhesion to target surfaces, including but not limited to endothelial, skeletal muscle, smooth muscle, and other mesenchymally-derived cells. For example, vascular grafts and stents may be coated with laminin 8 or pharmaceutical compositions thereof to stimulate endothelial cell attachment. Alternatively, bone or connective tissue grafts or prostheses may be coated with laminin 8 or pharmaceutical compositions thereof to stimulate adhesion of the appropriate cell type and improved grafting efficiency.

If the device is made of a natural or synthetic biodegradable material in the form of a mesh, sheet or fabric, laminin 8 or pharmaceutical compositions thereof may be applied directly to the surface thereof. Appropriate cells may then be cultured on the matrix to form transplantable or implantable devices, including dental abutment pieces, needles, metal pins or rods, indwelling catheters, colostomy tubes, surgical meshes and any other appliance for which coating with laminin 8 is desirable. Alternatively, the devices may be implanted and cells may be permitted to attach in vivo.

Coupling of the substantially purified laminin 8 may be non-covalent (such as by adsorption), or by covalent means. The device may be immersed in, incubated in, or sprayed with the laminin 8 or pharmaceutical compositions thereof.

The dosage regimen for various treatments using the laminin 8 of the present invention is based on a variety of factors, including the type of injury or condition, the age, weight, sex, medical condition of the individual, the severity of the condition, and the route of administration. Thus, the dosage regimen may vary widely, but can be determined routinely by a physician using standard methods. Laminins are extremely potent molecules, and one or a few molecules per cell could produce an effect. Thus, effective doses in the pico-gram per milliliter range are possible if the delivery is optimized. Laminins are sometimes present in an insoluble form in the basement membrane and have the capability of polymerizing at concentrations as low as about 50 μg/ml, depending on the laminin isoform and the conditions. Laminins can also polymerize into a gel at a concentration of about 2-3 mg/ml. Dosage levels of the order of between 1 ng/ml and 10 mg/ml are thus useful for all methods disclosed herein, preferably between about 1 μg/ml and about 3 mg/ml.

The present invention also provides a method for inducing cell attachment to the device (as disclosed above), comprising coating the appliance with laminin 8 or pharmaceutical compositions thereof prior to incubation with cells appropriate for the desired application.

Laminin preparations are known to induce the growth and differentiation of neurons (U.S. Patent No. 5,229,365), and have been used in combination with Type I collagen to coat a hollow conduit and promote nerve regeneration across a gap of severed nerve. (U.S. Patent No. 5,019,087)

Thus, in another embodiment, a method is provided for nerve regeneration, comprising administering to a subject in need thereof an amount effective of laminin 8 or pharmaceutical compositions thereof to promote nerve regeneration. The graft can comprise a nerve graft, or a prosthetic graft. Both bioresorbable and non-resorbable materials have been used in tubes for bridging nerve gaps. (See for example, Nyilas, et al., (Trans. Soc. Biomater., 6, 85, 1983), Molander, et al. (Biomaterials, Vol. 4, pp. 276-280, October, 1983), Colin, et al., (Journal of Dental Research July, 1984, pp. 987-993). The method can be used to treat diseases and injuries characterized by the loss of function and or/degeneration of neurons and nerves.

Laminins, or cell extracts containing laminins have been shown to regulate angiogenesis in a biphasic manner. (See, for example, Nicosia et al., Dev. Biol. 164:197-206 (1994); Bonfil et al., Int. J. Cancer 58:233-239 (1994)). At lower concentrations (30-300 μg/ml), a laminin-entactin complex stimulated angiogenesis in a three-dimensional culture, while at 3000 μg/ml the same complex was inhibitory to angiogenesis. Thus, in another aspect, the present invention provides methods for regulating angiogenesis, comprising contacting a tissue or culture substrate with an amount effective of laminin 8 or pharmaceutical compositions thereof to regulate angiogenesis. In one embodiments, the laminin 8 is used to promote angiogenesis by contacting a tissue or culture substrate with an amount effective of laminin 8 to promote angiogenesis. In another embodiment, the laminin 8 is used to inhibit angiogenesis, by contacting the tissue or culture substrate with an amount effective of laminin 8 to inhibit angiogenesis. An example of culture substrates to be contacted with laminin 8 to regulate angiogenesis are those used for tissue engineering purposes.

In another aspect of the present invention, laminin 8 is used for the culture of cells, including but not limited to endothelial cells, nerve cells, cells of hematopoietic lineage, and mesenchymally-derived cells including but not limited to cells derived from bone, connective tissue, and adipose tissue, skeletal muscle cells, and smooth muscle cells, by contacting the cells with an amount effective of laminin 8 to stimulate attachment and proliferation/differentiation/stasis of cells. The laminin 8 can either be provided in the cell culture medium, or as a cell culture medium supplement, or may be coated on the surface of a cell growth substrate. In a preferred embodiment, the method further includes contacting the cells with other compounds, including but not

limited to any of the collagens, other laminin types, fibronectin, α-dystroglycan, cadherins, integrins, entactin/nidogen, α-dystroglycan, glycoproteins, proteoglycans, heparan sulfate proteoglycan, glycosaminoglycans, epidermal growth factor or nerve growth factors, vascular endothelial growth factor, fibroblast growth factor, and peptide fragments thereof.

The cells may comprise primary cells or cell culture cell lines. The methods of this aspect of the invention can be used in vivo, ex vivo, or in vitro.

In a preferred embodiment, laminin 8 is used to coat the surface of a substrate, to promote cell adhesion to the substrate, and to stimulate cell proliferation/differentiation/stasis. The substrate used herein may be any desired substrate. For laboratory use, the substrate may be as simple as glass or plastic. For use in vivo, the substrate may be any biologically compatible material capable of supporting cell adhesion. Suitable substrate materials include shaped articles made of or coated with such materials as collagen, regenerated collagen, polyglycolic acid, polygalactose, polylactic acid or derivatives thereof; biocompatible metals such as titanium and stainless steel; ceramic materials including prosthetic material such as hydroxylapatite; synthetic polymers including polyesters and nylons; polystyrene; polyacrylates; polytetrafluoroethylene and virtually any other material to which biological molecules can readily adhere. The determination of the ability of a particular material to support adhesion of the r-laminin 8 of the invention requires only routine experimentation by the skilled artisan.

In a further aspect, the present invention provides cell growth substrates for adhesion and culturing of cells, by providing an amount effective of laminin 8 for the attachment of cells to a cell culture device for the attachment and subsequent proliferation/differentiation/stasis of the cells. The substrates may comprise any of the substrates discussed above.

In another aspect of the present invention, an improved cell culture medium is provided, wherein the improvement comprises addition to the cell culture medium of an effective amount of laminin 8 to the cell culture medium to promote the adherence, proliferation, and/or maintenance of cells. Any cell culture media that can support the growth of cells can be used with the present invention. Such cell culture media include, but are not limited to Basal Media Eagle, Dulbecco's Modified Eagle Medium, Iscove's

Modified Dulbecco's Medium, McCoy's Medium, Minimum Essential Medium, F-10 Nutrient Mixtures, Opti-MEM® Reduced-Serum Medium, RPMI Medium, and Macrophage-SFM Medium or combinations thereof.

The improved cell culture medium can be supplied in either a concentrated (ie: 10X) or non-concentrated form, and may be supplied as either a liquid, a powder, or a lyophilizate. The cell culture may be either chemically defined, or may contain a serum supplement. Culture media is commercially available from many sources, such as GIBCO BRL (Gaithersburg, MD) and Sigma (St. Louis, MO).In an alternative embodiment, the laminin 8 is used as a cell culture supplement.

The laminin 8 or pharmaceutical compositions thereof of the present invention can be used for the treatment of a variety of conditions and diseases as described herein, including but not limited to various vascular, neural, and mesenchymal tissue injuries, including but not limited to angioplasty restenosis, tissue ischemia, neural damage, vascular surgical procedures, atherosclerosis, bone fractures, defects, and disorders which result in weakened bones such as osteoporosis, osteoarthritis, and periodontal disease; bone loss resulting from cancer or side effects of other medical treatment; age-related loss of bone mass; articular cartilage tears, deformities and other cartilage defects such as arthritis and cartilaginous tissue damage, tendon or ligament tears, deformities and other tendon or ligament defects such as tendinitis and carpal tunnel syndrome, periodontal ligament injury, and tendon-to-bone detachment.

The amount of laminin 8 or pharmaceutical compositions thereof used in such treatments will, of course, depend upon the type and severity of the condition or disease being treated, the route of administration chosen, and will be determined by the attending physician or veterinarian. The term "therapeutically effective amount" of laminin 8 or pharmaceutical compositions thereof refers to the amount of laminin 8 or pharmaceutical compositions thereof, in the absence of other exogenously applied factors, determined to produce a therapeutic response in a mammal. Such therapeutically effective amounts are readily ascertained by one of ordinary skill in the art.

The present invention may be better understood with reference to the accompanying examples that are intended for purposes of illustration only and should

not be construed to limit the scope of the invention, as defined by the claims appended hereto.

EXAMPLES

Expression Constructs

For expression of the human laminin α4 chain containing a C-terminal FLAG epitope, the full length cDNA was constructed and modified as follows. Complementary DNA lambda clones subcloned into pBluescript™ or pCRscript™ (Stratagene) plasmid vectors from an earlier study (Iivanainen et al., 1995) were used as cDNA source, except for clone FL136. The EcoRI insert from FL136 lambda DNA was cloned into the pBluescript™ EcoRI site to make FL136E. The 0.78 kb SacI-BamHI fragment from clone FL76 was ligated into SacI-BamHI digested pSL1180 (Pharmacia) to make FL76SB. A sequence corresponding to nucleotides 2378-4274 of human laminin α4 cDNA was PCR-amplified using cDNA library as a template, digested with SacI and cloned into the FL76SB SacI site and its orientation confirmed to make HL4-SB. The FL64 BamHI-SalI fragment was cloned into HL4-SB BamHI-SalI to make HL4-3'.

The Eco72I-XhoI fragment from clone FL117 was ligated into the Eco72I-XhoI sites of FL136E to make HL4-5'. Both mouse and human laminin α4 cDNAs have poorly conserved Kozak-sequences at the translation initiation site, as well as several extra 5' untranslated region (UTR) ATG sequences. To ensure efficient and correct translation initiation, the Kozak sequence was edited to match the consensus and the rest of the 5' UTR was deleted using standard molecular biology techniques. The resulting product was EcoRI-EagI-digested and cloned to the EcoRI-EagI-digested HL4-5' to make HL4Mut-5'. The SpeI-XhoI fragment from HL4Mut-5' was cloned into HL4-3' to make clone HL4-Full with full length cDNA. The EcoRI insert from HL4-Full was cloned into pcDNA3.1/Zeo(-) expression vector (Invitrogen) to make HL4-Full.pcDNA. (SEQ ID NO:1)

The sequence encoding the FLAG epitope (SEQ ID NO:3) was inserted as follows. The FL64 BamHI-HindIII fragment was cloned into pUC19 to make FL64BH. PCR was performed using primers to introduce the FLAG epitope, using HL4-3' as template. The product was digested with XbaI and HindIII and cloned into

XbaI-HindIII digested FL64BH to make HL4FLAG-3'. This also resulted in deletion of the original 3' UTR. The BamHI-HindIII fragment from HL4FLAG-3' was cloned into BamHI-HindIII-digested HL4-Full.pcDNA vector, replacing the original BamHI-HindIII fragment to make HL4FLAG-B, which lacked the BamHI-BamHI fragment. The final expression construct named HL4FLAG-Full was made by inserting the missing BamHI fragment in the correct orientation. All PCR-derived parts of the cDNA sequence were sequenced to ensure that no mutations had occurred during amplification.

The construct used for expression of the mouse laminin β1 chain (SEQ ID NO:15) has been previously described (Yurchenco et al., *Proc. Natl. Acad. Sci. U. S. A.* 94(19), 10189-94 (1997)).

To make the construct named HG1 for expression of the human laminin γ1 chain, full length cDNA (SEQ ID NO:19) encoding the human laminin γ1 chain was released with BamHI from a baculovirus expression vector pVL941 (unpublished) and cloned into the BamHI site of a pcDNA3.1/Hygro(-) mammalian expression vector (Invitrogen).

Antibodies, control proteins, and cell lines

Affinity purified polyclonal anti-laminin α4 antibody (Ab) S8 was prepared as described previously. (Iivanainen et al., 1997, *J. Biol. Chem.* 272(44), 27862-8) Polyclonal anti-EHS-laminin Ab, anti-FLAG M2 monoclonal Ab (mAb), purified control mouse IgG, RGDS-peptide and heparin (grade I-A) were purchased from Sigma Chemical Company (St. Louis, MO). Anti-laminin γ1 (clone 22) mAb was from Transduction Laboratories (Lexington, KY). Mouse function blocking mAbs against integrin α1 (clone FB12), integrin α2 (clone P1E6), and integrin α3 (clone P1B5) were obtained from Chemicon (Temecula, CA). Rat function blocking mAbs anti-integrin α6 (clone GoH3) and control rat IgG_{2a} were also from Chemicon. Rat function blocking mAbs against integrin α5 (clone BIIG2) and integrin β1 (clone AIIB2) were provided by Dr. C. Damsky (Univ. of California, San Francisco) as hybridoma supernatants. Immunoglobulins were purified from the supernatants using GAMMABIND PLUS™ Sepharose (Pharmacia; Stockholm, Sweden) according to the manufacturer's instructions. Secondary Ab conjugates anti-rabbit IgG-HRP and anti-

mouse IgG-HRP were from Dakopatts (Denmark). Laminin 1 from EHS-tumor, collagen type IV from EHS-tumor, and human placental laminin were obtained from Sigma. Fibronectin and some of the laminin 1 from EHS-tumor were purchased from Gibco BRL (Rockville, MD) EHS-derived laminin 1/nidogen complex was kindly provided by Dr. J. Engel (Univ. of Basel, Switzerland). Human fibrosarcoma HT-1080 (CCL-121) cells were from the American Type Tissue Collection. (Manassas, VA) IMMORTOMOUSE™ brain capillary endothelial (IBE, Kanda et al., 1999, *Exp. Cell Res.* 248(1), 203-13) and bovine adrenal microvascular (BCE, Folkman et al., 1979) cells were kindly provided by Dr. L. Claesson-Welsh (Medical Biochemistry and Microbiology, Univ. of Uppsala) and K. Olausson (Medical Cell Biology, Univ. of Uppsala). Three human erythroleukemic K562 cell lines transfected to express integrins α3 (Delwel et al., 1994, *Mol. Biol. Cell* 5(2),203-15), α6 (Delwel et al., 1993, *J. Biol. Chem.* 268(34), 25865-75), or both α6 and α4 (Niessen et al., 1994, *Exp. Cell Res.* 211(2), 360-7 *Mol. Biol. Cell*) were provided by Dr. A. Sonnenberg (Netherlands Cancer Institute, Amsterdam, Netherlands).

Production and purification of recombinant laminin 8

Recombinant laminin 8 ("r-laminin 8") was produced in human embryonic kidney cells (HEK-293, ATCC CRL-1573) cultured in DME/pyruvate/10% fetal calf serum (FCS) at 37°C in a humidified 5% CO_2 atmosphere. Wild-type cells were stably transfected with the laminin β1 expression construct as previously described (Yurchenco et al., 1997) and selected using 500 μg/ml G418. All further cell culture and clonal expansion was carried out in the continuous presence of relevant selection antibiotics. A highly expressing clone was then transfected with the HL4FLAG-Full construct using standard calcium-phosphate transfection methods, and stable colonies were selected using 300 μg/ml Zeocin. Clones were isolated using cloning rings, expanded, and analyzed for laminin α4 secretion by Western blotting of medium using the anti-laminin α4 Ab S8. The clone with the highest expression was transfected with the HG1 construct, and stable clones were selected using 100 μg/ml hygromycin. These clones were then screened via Western blotting using a mAb against laminin γ1, and clones showing the highest secretion were expanded further.

For production of r-laminin 8, cells were grown in the culture medium for up to four days, after which the medium was collected and centrifuged to remove cell debris. After collection, Tris-Cl pH 7.5 was added to 50 mM and EDTA was added to a concentration of 10 mM. If not used immediately, the medium was stored at -70°C. For protein production into serum-free medium, confluent cultures were washed twice with PBS and the medium was changed to DME supplemented with pyruvate, insulin-transferrin-selen supplement (Sigma) and 1 μg/ml aprotinin (Sigma).

r-laminin 8 was affinity purified using an anti-FLAG M2 matrix (Sigma). Before use, the matrix was washed with 0.1M glycine (pH 3.5) and TBS (50 mM Tris-HCl pH 7.5/150 mM NaCl) according to the manufacturer's instructions. Brij-20 (Fluka, Milwaukee, Wisconsin) was added to the medium to a final concentration of 0.05% (v/v), and the medium was incubated in batch mode with the matrix (25 μl matrix/ml) overnight at 4°C with agitation. The matrix was collected by passing the medium through a sintered column, and washed extensively in the column first with TBS/1 mM EDTA and then PBS/1 mM EDTA. Bound r-laminin 8 was competitively eluted with 100 μg/ml FLAG peptide (Sigma) in PBS/1mM EDTA at room temperature. The matrix was then regenerated as recommended by the manufacturer. The eluate was diluted 1:1 with 20 mM $NaPO_4$/1 mM EDTA (pH 7.5), and injected into a UNO-Q ion-exchange column (Bio-Rad, Hercules, CA). At this salt concentration, the FLAG peptide passes through, but r-laminin 8 is bound. The column was then washed with 20 mM phosphate/1 mM EDTA, and the r-laminin 8 was eluted with 20 mM $NaPO_4$/1.5M NaCl/1 mM EDTA. The eluate was diluted 1:10 with 20 mM $NaPO_4$ (pH 7.5)/1 mM EDTA to a final salt concentration of 150 mM and concentrated using 100 kD cut-off ultrafiltration (Gelman; Ann Arbor, Michigan) to approximately 0.5 mg/ml.

Characterization of r-laminin 8

Secreted r-laminin 8 in cell medium and after purification was characterized using linear 5% or 6% SDS-PAGE and 3-12% gradient SDS-PAGE under reducing and non-reducing conditions. Proteins were visualized using silver staining or blotted to PVDF membranes using a semi-dry blotting system (Bio-Rad). For immunodetection, Renaissance ECL-System (Dupont, Waltham, MA) was used in conjunction with the

Abs described above. Protein quantitation was done by measuring absorbance at 280 nm or using the Bradford method (Bio-Rad protein assay kit).

Rotary shadowing electron micrography (EM) was performed as described previously. (Yurchenco and Chen, 1993) When purifying for rotary shadowing, the matrix was equilibrated with 0.15 M NH_4HCO_3-acetate buffer (pH 7.4), and the r-laminin 8 was then eluted with FLAG-peptide in the same buffer.

Adhesion assays and cell culture

For adhesion assays, flat-bottom 96 well plates (Maxi-Sorp, Nunc; Rochester, NY) were coated by incubating with proteins diluted in PBS overnight at 4°C (50 µl/well). The remaining protein-binding capacity was saturated by addition of 2% heat-inactivated BSA in PBS (50 µl/well) and further incubation for at least 4 hours. Prior to assaying, the coating/blocking solution was aspirated, and the wells were washed with the binding medium (100 µl/well). Drying of coated protein was avoided, since this was found to be detrimental to adhesion in some cases.

All cells were cultured in humidified 5% CO_2 atmosphere. HT-1080 and BCE cells were cultured in DME/10% FCS/pyruvate at 37°C, BCE on gelatin-coated plastic. IBE cells were cultured in F12/10% FCS/2 U/ml γ-interferon on gelatin-coated plastic at 33°C. Transfected K562 cells were grown in suspension in RPMI/10%FCS supplemented with 1 mg/ml G418 at 37°C. For K562 cells transfected with both α4 and β4 integrins, 0.7 mg/ml hygromycin was included in the medium. Prior to dissociation, the cells were washed twice with PBS. HT-1080 cells were disassociated using 5 mM EDTA in PBS, while the others were disassociated using trypsin-EDTA (Gibco-BRL). To remove trypsin, cells were pelleted and resuspended twice in serum-free medium. Cells were counted and suspended in buffered serum-free medium at 2-3 x 10^5 cells/ml. K562 cells were washed twice with serum-free medium and resuspended at 10^6 cells/ml. DME/25 mM HEPES/pyruvate was used for HT-1080 cells; F12/25 mM HEPES/0.25% BSA was used for other cell types.

K562 cell stimulation was done using 5 ng/ml PMA (Sigma). Antibodies or other test compounds were added to the cell suspension and the cells were allowed to recover at 37°C for 30 minutes. The cells were then added to the protein-coated 96-

well plates (100 µl/well) and allowed to adhere for 30 (K562) or 60 (other cells) minutes at 37°C. To remove unbound cells, wells were washed by two or three cycles of careful addition of 100 µl of binding medium followed by aspiration. The remaining cells were fixed with 1% glutaraldehyde in PBS for 10 minutes at room temperature. Cells were stained with 0.1% crystal violet (Sigma) for 30 minutes and unbound stain was removed by four washes with water. Bound stain was solubilized in 2% SDS (100 µl/well) and quantitated by measuring the absorbance at 595 nm using a microplate reader.

None of the cell lines bound appreciably to BSA. When the quantitative results were calculated, binding to BSA was given a value of zero, while the relevant control was given the value of 100. The mean and SEM were calculated from results obtained from parallel wells.

RESULTS

Production and characterization of r-laminin 8

Unconcentrated medium from wild-type HEK-293 cells did not react in Western blots with the anti-laminin α4, anti-laminin γ1, anti-EHS-laminin, or anti-FLAG antibodies, indicating that these cells express endogenous laminins at very low amounts if at all. The transfected α4 chain could be secreted to some extent even when expressed alone, but secretion of the other chains required simultaneous expression of all three chains. Cells transfected with laminin α4, β1, and γ1 chain expression constructs secreted large amounts of all three chains to the medium. The best cell clones ("G1-2" and "G1-3") were estimated to produce 3-5 milligrams or r-laminin 8 per liter of medium.

The r-laminin 8 bound to anti-FLAG M2 matrix with high specificity. When eluted competitively with the FLAG peptide, only laminin α4, β1, and γ1 bands were seen in silver-stained 3-12% gradient SDS-PAGE gels. (Figure 1) Under non-reducing conditions, the purified protein hardly entered the gel, which was to be expected as the predicted molecular weight for the mature trimer is at least 570 kD. A minor fraction of the purified trimer appeared as non-covalently associated (see discussion). In this fraction, the β1 and γ1 chains appeared as covalently associated dimers, whereas the α4 chain was non-covalently associated. Under reducing conditions, the protein appeared

as a broad band at around 200 kD, which reacted on Western blots with α4, EHS, γ1, and anti-FLAG antibodies. The predicted molecular weights for mature α4, β1, and γ1 polypeptides are 200, 195, and 174 kD respectively. Laminins are heavily glycosylated, which may account for the slight discrepancy in molecular weight observed in SDS-PAGE. The β1 and γ1 chains of laminin 1 purified from EHS-tumor showed similar or slightly slower mobility than those of r-laminin 8.

Rotary shadowing EM revealed r-laminin 8 to be a Y-shaped molecule with two short and one long arm in accordance with the predicted structure. (Figure 2) In many cases, a very short (5-10 nm) rod-like stub could be seen at the junction of the arms. The G-domains could sometimes be seen as consisting of two moieties.

Cell binding to r-laminin 8 and receptor identification

We assayed the binding of human fibrosarcoma (HT-1080) and transfected K562 cells to r-laminin 8 in the presence of different blocking anti-integrin antibodies to identify integrin receptors binding to r-laminin 8. Immortomouse brain capillary endothelial (IBE) and bovine adrenal microvascular endothelial (BCE) cells were also used to study the adhesion of endothelial cells to r-laminin 8. The BCE cells express at least integrins α6β1, α6β4, α1β1, α2β1, α3β1, α5β1, αvβ1, αvβ3, and α5β5 (Klein et al., 1993, *Mol. Biol. Cell* 4(10), 973-82), whereas IBE cells have been reported to express integrins α3, α5 and β1, but not α1, α2, or α6 (Kanda et al., 1999)

When compared to laminin 1, the adhesiveness of r-laminin 8 was quantitatively similar or slightly weaker for the cell lines studied, as approximately the same number of cells bound to both substrates after washing. (Figure 3) Similar results were obtained with IBE and BCE cells (data not shown). In further cell adhesion assays (Figures 4-8), cells were allowed to bind to either-laminin 8 or laminin 1 coated at 10 μg/ml on 96 well plates. Prior to the assay, different components were added to the cell medium. Values indicated are relative to that of control antibody (normal mouse IgG for mouse antibodies and rat IgG_{2a} for rat monoclonal antibodies), which was designated as 100. For other substances, the same volume of buffer was added. Adhesion to bovine serum albumin (BSA) was designated zero. The text under the columns indicate the integrin subunit blocked or the added substance. Error bars

indicate SEM. Integrin monoclonal antibodies were used at 10 μg/ml, heparin at 2 mg/ml, and EDTA at 5 mM.

Monoclonal antibodies against integrins α1 and α2 were tested only in the HT-1080 cell line, where they had no or only small effects on cell binding, indicating that these integrins were not major mediators of adhesion to r-laminin 8 (Figure 4). Adhesion to Type IV collagen was reduced to about 50% by the anti-integrin α2 mAb, demonstrating the presence of active α2 integrin (data not shown). Integrin α1 mAb had only a slight effect on adhesion to collagen IV when used alone, but it had a synergistic effect when used in combination with the α2 mAb (not shown). The Ab against integrin α3 had only minor effects on adhesion of HT-1080 when used alone, but it had a synergistic effect when used in combination with the α2 mAb (data not shown). The monoclonal antibody to α2 integrin had only minor effects on adhesion of HT 1080 (Figure 4) cells to fibronectin or laminin, even though the cells have been shown to express high levels of α3β1 (Wayner et al., 1993, *J. Cell Biol.* 121(5), 1141-52). The blocking of integrin α5 had a slight stimulating effect on HT-1080 adhesion to both laminin 1 and laminin 8 (Figure 4), whereas adhesion of BCE cells to r-laminin 8 was slightly reduced (Figure 5). The mAb did block adhesion of HT-1080 cells to fibronectin almost completely, indicating the presence of active α5 integrin in these cells (not shown).

α-6 subunit containing integrin(s) were identified as the major mediators of adhesion to r-laminin 8. The integrin α6 subunit is known to associate with either β1 or β4 (Sonnenberg et al., 1990, *J. Cell Sci.* 96(Pt 2), 207-17). By using a mAb (GoH3) that blocks α6β1- and α6β4-mediated binding, we could completely abolish binding of HT-1080 and BCE cells to r-laminin 8. An anti-β1 integrin mAb (AIIB2) also completely blocked the binding of HT-1080 cells to r-laminin 8 indicating that integrin α6β1 is crucial for adhesion of these cells to r-laminin 8 (Figure 4). In contrast, binding of BCE cells was blocked only partially (about 70%) by the anti-β1 mAb, suggesting that these endothelial cells use both α6β1 and α6β4 to adhere to r-laminin 8 (Figure 5). In another endothelial cell line, the mouse IBE cells, the anti-α6 subunit mAb blocked the binding to r-laminin 8 only partially (about 60%), suggesting that the

cells are using, in addition to α6-subunit containing integrins, also other receptors (Figure 6).

Interestingly, when adhesion to r-laminin 8 was compared to that of laminin 1, it was observed that the adhesion was quite differently affected by the blocking anti-α6 and anti-α1 integrin mAbs. HT-1080 cells interacted with laminin 1 not only via α6β1 integrin, but also via other β1-subunit-containing integrin(s), since the blocking was only partial with anti-α6, but complete with anti-β1. (Figure 4) Furthermore, the adhesion of BCE cells to laminin 1 was mediated by β1 integrin(s) other than α6β1, since the adhesion was completely blocked by anti-β1, but was only minimally affected by anti-α6. (Figure 5) Similarly, in IBE cells, the adhesion to laminin 1 was mediated by receptors other than α6 integrin(s), since it was not affected by anti-α6. (Figure 6)

To verify the role of α6β1 and α6β4 integrins as r-laminin 8 receptors, transfected K562 cells were used. Parental K562 cells endogenously express only integrin α5β1, which is in an inactive state. The cells normally grow in suspension but can be made adherent with an activating anti-β1 Ab or stimulation with PMA. K562 cells transfected with the α6 subunit express α6β1 on the cell surface (Delwel et al., 1993). Interestingly, while these cells bound laminin 1 efficiently only after stimulation with PMA, they bound r-laminin 8 strongly even without stimulation (Figure 8). This finding demonstrates that the adhesive properties of r-laminin 8 are different from those of laminin 1. The cell adhesion to both laminin isoforms could be blocked with either anti-integrin α6 or β1 mAbs, which agrees with results obtained with other cell lines (Figure 4-5). In addition to inactive α6β1, K562 cells transfected with α6 and β4 subunits express constitutively active α6β4 complex, and can bind laminin 1 even without stimulation (Niessen et al., 1994). We found that these cells bound to both laminin 1 and laminin 8 without stimulation, although activation of the β1 integrins with PMA resulted in increased adhesion. The adhesion of non-stimulated cells could be completely inhibited with anti-integrin α6, but only partially with anti-β1, again indicating that α6β4 is able to mediate adhesion to r-laminin 8 (Figure 7). In contrast, K562 cells expressing α3β1 adhered poorly to both laminin isoforms (not shown). This agrees with an earlier study where α3-transfected K562 cells were found to bind efficiently to laminin 8, but poorly to laminin 1 (Delwel et al., 1994).

Cell adhesion to both laminin 1 and r-laminin 8 was found to be dependent on divalent cations, since it could be abolished by 5 mM EDTA in all cell lines tested (Figures 4-8). Heparin, when used at 2 mg/ml, had no effect on the adhesion of HT-1080, BCE, and IBE to r-laminin 8 (Figures 4-6). On laminin 1, however, there was a slight decrease in adhesion of BCE cells (Figure 5), while the other cell lines were unaffected (Figures 4,6). The RGDS-peptide that is reported to block the function of various integrins (Pierschbacher and Ruoslahti, 1984, *Nature* 309(5963), 30-3) had no effect at 1 mM concentration on adhesion of HT-1080, BCE, or IBE cells to the laminins (data not shown).

It was further observed that the cell-binding activity of r-laminin 8 was sensitive to air-drying. When the coated protein was allowed to air dry for 15 minutes at room temperature before adding the cells, the cell-binding activity of r-laminin 8 was completely lost (Figure 4). Even shorter than a 15 minute exposure could abolish the cell-binding activity (not shown). A drop of buffer was allowed to sit on the plastic, while the rest of the well was briefly exposed to air drying. On the dried area, the BCE cells were rounded, and only a few of them showed any signs of spreading. On the area kept wet, practically all cells were well spread and tightly adhered to the surface. Accordingly, all cells on the dried area were lost during washing. Laminin 1 was not as sensitive to this effect, but drying still reduced the cell binding activity by half (Figure 4).

DISCUSSION

The present work provides significant advances concerning the recently described laminin 8 isoform and its α4 chain. Large quantities or r-laminin 8 could be produced as native trimeric protein in cultured human cells, and the r-laminin 8 was shown to be biologically active and to have cell adhesive properties. Furthermore, r-laminin 8 was shown to have a preference for binding to the α6 integrins.

The r-laminin 8 produced in this study is a species hybrid of two human (α4 and γ1) and one mouse (β1) chains, and it contained a FLAG epitope tag attached to the C-terminus of the α4 chain. Despite these modifications, r-laminin 8 assembled into trimers in a manner expected from a native laminin protein, as demonstrated by rotary shadowing EM. The amount of r-laminin 8 produced by the HEK-293 cells in

monolayer cultures was quite high considering the size and complexity of the protein. An amount of 3-5 mg/L of culture medium is similar to what is frequently obtained in eukaryotic systems, such as the baculovirus insect cell system.

Similarly to other laminin isoforms characterized to date, all the chains of the r-laminin 8 trimer were disulfide linked to each other. Only a minor fraction consisted of disulfide-linked β1/γ1 containing dimers and non-crosslinked α4. These chains were also associated into trimers, since the dimers followed the FLAG-tagged α4 chain in immunoprecipitations using the anti-FLAG mAb. The presence of the α4 chain in r-laminin 8 trimers was also demonstrated by showing that all of the α4 could be immunoprecipitated after several rounds of immunoprecipitation with the anti-laminin 1 Ab that recognizes the α1, β1, and γ1 chains (data not shown).

The reason for the two minor r-laminin 8 bands of different size reacting with EHS and γ1 antibodies is unclear. The larger one agrees with the size for a dimer, but the smaller one could not be accounted for. The size difference could be as large as 100 kD. It is possible that these dimers and non-covalent trimers are the products of incomplete or incorrect post-translational processing due to overexpression.

The purified r-laminin 8 was shown to have biological activity, as all cell lines tested in this study adhered to and spread equally well on r-laminin 8 as on laminin 1. This activity could be abolished by drying the protein, suggesting that native conformation was important for full cell binding activity. The cell binding in all cases be abolished by EDTA, indicating dependence on divalent cations.

A large variety of integrins have been implicated as receptors for different laminin isoforms. In this study, we demonstrated that integrins α6β1 and α6β4 were major mediators of cell adhesion to r-laminin 8. The adhesion of HT-1080 and BCE cells was completely blocked by anti-integrin α6 mAb, despite the fact that both cell lines express a wide spectrum of β1 and αv integrins, including several of those shown to bind to other laminin isoforms. (Conforti et. al., 1994, *Cell Adhes. Commun.* 1(4), 279-93) HT-1080 cell adhesion to r-laminin 8 is mediated solely by integrin α6β1, since the adhesion could be blocked not only by anti-α6 mAb, but also by the β1 antibody. In contrast, the β1 mAb only partially blocked adhesion to BCE cells, suggesting that α6β4 contributed to the binding of BCE cells to r-laminin 8. The role

of α6β4 as a r-laminin 8 receptor was confirmed by assaying the binding of α6 and β4 transfected K562 cells that express both α6β1 and α6β4 on the cell surface. Indeed, adhesion was completely blocked with α6 mAb, but only partially with β1 mAb, indicating that the α6β4 complex also binds to r-laminin 8. K562 cells expressing α6β1 bound r-laminin 8 while α3β1 expressing cells did not, thus confirming that integrin α6β1 binds r-laminin 8. Our results somewhat contradict the reported lack of integrin α6 subunit in IBE cells (Kanda et al, 1999), since the adhesion to r-laminin 8 was severely perturbed by the anti-integrin α6 mAb. The result suggests that these cells use yet another receptor(s) in addition to α6 integrins for binding to r-laminin 8. However, in certain cases GoH3 is not able to completely block integrin α6 in α6β4 complexes (Sonnenberg et al., 1993, *J. Cell Sci.* 106(Pt 4), 1083-102). Thus, the remaining adhesion could be due to incompletely blocked α6β4 complexes.

Interestingly, adhesion of the cell lines tested to r-laminin 8 was found to be more dependent on integrin α6 than adhesion of the cell lines to laminin 1. Another indication of the different adhesive properties of r-laminin 8 and laminin 1 was the finding that α6β1-expressing K562 cells did bind to r-laminin 8 without stimulation, but, as also previously reported (Delwel et al., 1993), needed to be stimulated by PMA to efficiently bind to laminin 1 coated surfaces. Thus, r-laminin 8 appears to have a higher avidity or affinity than laminin 1 to α6β1. The α6β1 integrin might bind r-laminin 8 even in the conformation that makes it unable to bind to laminin 1, or the cells could be stimulated by the presence of r-laminin 8 via an unknown mechanism. It could be that the avidity/affinity difference is of biological significance, and may well be one reason for the existence of large numbers of laminin isoforms.

In addition to integrins, several other cell surface proteins have been reported to function as laminin receptors. Alpha-dystroglycan is a component of the dystrophin-dystroglycan complex in the skeletal muscle thought to connect the contractile cytoskeleton to the extracellular matrix. Dystroglycan has also been shown to bind laminin 2 and dystrophin, forming a link between the two. (Ervasti and Campbell, 1993, *J. Cell Biol.* 122(4), 809-23) Indirect evidence suggests that laminin 8 might bind to α-dystroglycan; it has been shown that laminin from laminin αd-deficient dystrophic muscle bound dystroglycan, but, in contrast to laminin from normal muscle,

in a manner that was sensitive to inhibition by heparin. (McDearmon et al., 1998, *J. Biol. Chem.* 273(37), 24139-44) Since upregulation of laminin α4 has been observed in laminin α2 deficient muscular dystrophy (Patton et al, 1997; Ringelmann et al., 1999), it can be assumed that the laminin α4 chain is involved in the observed interaction. Alpha-dystroglycan is not restricted to skeletal muscle. (Durbeej et al. 1998, *J. Histochem. Cytochem.* 46(4), 449-57) It was recently shown to be a receptor for laminin 1 in bovine aorta endothelial cells, binding in a manner sensitive to heparin, dextran sulfate, and fucoidan. (Shimizu et al., 1999, *J. Biol. Chem.* 274(17), 11995-2000) Heparin-sensitive interactions were not detected in this study, but this does not rule out the possibility of such interactions in other cell types or in vivo. We did observe that the r-laminin 8 binds heparin-sepharose at physiological salt concentration (data not shown).

In this study, integrins α6β1 and α6β4 were identified as receptors for r-laminin 8 in cultured cells, and thus it is likely that these integrins mediate binding of laminin 8 in vivo, such as to endothelial and muscle cells. Endothelial cells express a wide variety of integrins depending on developmental stage, activation state, and location. At least integrins α2β1, α5β1, α6β1, α6β4, and αvβ3 have been found in endothelial cells in vivo (Sonnenberg 1990; Conforti 1992), whereas the main laminin isoforms in endothelial basement membranes (BM) are laminins 8 and 10. Other cells besides endothelial cells are likely to interact with the laminin 8 in endothelial BM; platelets contain and secrete laminin 8 when stimulated and adhere to it using the α6β1 intregrin.

Laminins 8 and 9 are also found in developing muscle and in the peripheral nervous system, overlapping in expression with integrin α6. In laminin α2-deficient muscle, both the laminin α4 and integrin α6 are upregulated. (Vachon et al, 1997, *J. Clin. Invest.* 100(7), 1870-81) Interestingly, integrin α6 and integrin β4 knock-outs result in epidemolysis bullosa (Georges-Labouesse et al, 1996, *Nat. Genet.* 13(3), 370-3; van der Neut et al., 1996, *Nat. Genet.* 13(3), 366-9), but no muscular or vascular phenotype was reported.

The present invention is not limited by the aforementioned particular preferred embodiments. It will occur to those ordinarily skilled in the art that various modifications may be made to the disclosed preferred embodiments without diverting

from the concept of the invention. All such modifications are intended to be within the scope of the present invention.

We claim

1. Substantially purified laminin 8.

2. The substantially purified laminin 8 of claim 1, comprising recombinant laminin 8.

3. The substantially purified recombinant laminin 8 of claim 2 comprising:

a first chain comprising a polypeptide that is substantially similar to an α4 laminin chain;

a second chain comprising a polypeptide that is substantially similar to a β1 laminin chain; and

a third chain comprising a polypeptide that is substantially similar to a γ1 laminin chain;

wherein the first, second, and third chains are assembled into recombinant heterotrimeric laminin 8.

4. The substantially purified recombinant laminin 8 of claim 2 comprising:

a first chain encoded by a polynucleotide that hybridizes under high stringency conditions to a coding region of one or more of SEQ ID NO:1, 3, 5, 7, 9, or fragments thereof;

a second chain encoded by a polynucleotide that hybridizes under high stringency conditions to a coding region of one or more of SEQ ID NO:11, 13, 15, 17, or fragments thereof; and

a third chain encoded by a polynucleotide that hybridizes under high stringency conditions to a coding region of one or more of SEQ ID NO: 19, 21, 23, 25, or fragments thereof;

wherein the first, second, and third chains are assembled into recombinant heterotrimeric laminin 8.

5. The substantially purified recombinant laminin 8 of claim 2 comprising:

a first chain comprising a polypeptide at least 70% identical to one or more of SEQ ID NO:2, 4, 6, 8, 10 or fragments thereof;

a second chain comprising a polypeptide at least 70% identical to one or more

of SEQ ID NO:12, 14, 16, 18 or fragments thereof; and

a third chain comprising a polypeptide at least 70% identical to one or more of SEQ ID NO:20, 22, 24, 26, or fragments thereof;

wherein the first, second, and third chains are assembled into recombinant heterotrimeric laminin 8.

6. The substantially purified recombinant laminin 8 of claim 2 comprising a first, second, and third polypeptide chain, wherein the first, second, and third polypeptide chains each comprise a general structure selected from the group consisting of: (1) R1-R2-R3; (2) R1-R2-R3(e); (3) R3; (4) R3(e); (5) R1-R3; (6) R1-R3(e); (7) R2-R3; and (8) R2-R3(e)

wherein R1 is a amino terminal methionine; R2 is a signal sequence that is capable of directing secretion of the polypeptide, wherein the signal sequence may be the natural signal sequence for the particular laminin chain, that of another secreted protein, or it may be an artificial sequence; R3 is a secreted α4 laminin chain for the first polypeptide chain, a secreted β1 laminin chain for the second polypeptide chain, and γ1 laminin chain for the third polypeptide chain; and R3(e) is identical to R3, but further comprises an epitope tag.

7. Recombinant laminin 8-expressing host cells.

8. The recombinant laminin 8-expressing host cells of claim 7, wherein the cells express recombinant laminin 8 comprising:

a first chain comprising a recombinant polypeptide that is substantially similar to an α4 laminin polypeptide;

a second chain comprising a recombinant polypeptide that is substantially similar to a β1 laminin polypeptide sequence; and

a third chain comprising a recombinant polypeptide that is substantially similar to a γ1 laminin polypeptide sequence;

wherein the cell expresses the first, second, and third chains, and wherein the first, second, and third chains assemble into recombinant laminin 8 that is secreted into the media by the cultured cell.

9. The recombinant laminin 8-expressing host cells of claim 7, wherein the cells express recombinant laminin 8 comprising:

a first chain encoded by a polypeptide that hybridizes under high stringency conditions to a coding region of one or more of SEQ ID NO:1, 3, 5, 7, or 9, or fragments thereof;

a second chain encoded by a polypeptide that hybridizes under high stringency conditions to a coding region of one or more of SEQ ID NO:11, 13, or fragments thereof; and

a third chain encoded by a polypeptide that hybridizes under high stringency conditions to a coding region of one or more of SEQ ID NO: 15, 17, or fragments thereof;

wherein the cell expresses the first, second, and third chains, and wherein the first, second, and third chains assemble into recombinant laminin 8 that is secreted into the media by the cultured cell.

10. The recombinant laminin 8-expressing host cells of claim 7, wherein the cells express recombinant laminin 8 comprising:

a first chain comprising a polypeptide at least 70% identical to one or more of SEQ ID NO:2, 4, 6, 8, 10 or fragments thereof;

a second chain comprising a polypeptide at least 70% identical to one or more of SEQ ID NO:12, 14, 16, 18 or fragments thereof; and

a third chain comprising a recombinant polypeptide at least 70% identical to one or more of SEQ ID NO:20, 22, 24, 26, or fragments thereof;

wherein the cell expresses the first, second, and third chains, and wherein the first, second, and third chains assemble into recombinant laminin 8 that is secreted into the media by the cultured cell.

11. The recombinant laminin 8-expressing host cells of claim 7, wherein the cells express recombinant laminin 8 comprising a first, second, and third polypeptide chain, wherein the first, second, and third polypeptide chains each comprise a general

structure selected from the group consisting of: (1) R1-R2-R3; (2) R1-R2-R3(e); (3) R3; (4) R3(e); (5) R1-R3; (6) R1-R3(e); (7) R2-R3; and (8) R2-R3(e)

wherein R1 is a amino terminal methionine; R2 is a signal sequence that is capable of directing secretion of the polypeptide, wherein the signal sequence may be the natural signal sequence for the particular laminin chain, that of another secreted protein, or it may be an artificial sequence; R3 is a secreted α4 laminin chain for the first polypeptide chain, a secreted β1 laminin chain for the second polypeptide chain, and γ1 laminin chain for the third polypeptide chain; and R3(e) is identical to R3, but further comprises an epitope tag .

12. The host cells of any of claims 7-11, wherein the host cell is a mammalian cell.

13. The host cells of claim 12, wherein at least one of the first, second, or third chains is expressed as a fusion protein with an epitope tag.

14. A method of purifying recombinant laminin 8, comprising:

a. providing the host cells of claim 12;

b. growing the cells in cell culture medium under conditions to stimulate expression of the recombinant laminin 8 chains;

c. passing the cell culture medium through an affinity chromatography column, wherein the column contains a compound that binds to the recombinant laminin 8;

d. washing the affinity column to remove unbound materials; and

e. eluting the bound recombinant laminin 8 from the column.

15. Substantially purified recombinant laminin 8 isolated according to the method of claim 14.

16. A pharmaceutical composition comprising:

a. laminin 8; and

b. a pharmaceutically acceptable carrier.

17. The pharmaceutical composition of claim 16, wherein the laminin 8 comprises recombinant laminin 8.

18. A method to accelerate healing of a vascular tissue injury in a subject, comprising contacting the site of the vascular tissue injury of the subject with an amount effective of laminin 8 to promote re-endothelialization at the vascular tissue injury site.

19. The method of claim 18, wherein the vascular injury is selected from the group consisting of angioplasty restenosis, vascular surgical procedures, aneurysm, and atherosclerosis.

20. A method to accelerate healing of a bone or connective tissue injury in a subject comprising contacting the site of the bone or connective tissue injury in the subject with an amount effective of laminin 8 to accelerate healing of the bone or connective tissue injury.

21. The method of claim 20 wherein healing is accomplished by incorporation of recombinant laminin 8 into wound repair dressings, matrices, or tissue grafts.

22. The method of claim 20 wherein the bone or connective tissue injury is selected from the group consisting of fractures, tears, deformities, or defects of bone, tendon, cartilage, and ligament.

23. A method to improve the biocompatibility of a medical device or graft, comprising contacting the medical device or graft with an amount effective of laminin 8 to improve the biocompatibility of the medical device or graft.

24. An improved medical device or graft, wherein the improvement consists of providing a medical device or graft with an amount effective of laminin 8 to improve the biocompatibility of the medical device or graft.

25. A method to regulate angiogenesis in a subject, comprising contacting a site in need of angiogenesis in the subject with an amount effective of laminin 8 to regulate angiogenesis.

26. A method to promote neural regeneration in a subject, comprising contacting a site in need of neural regeneration in the subject with an amount effective of laminin 8 to promote neural regeneration.

27. A method to promote cell adhesion to a surface, comprising contacting cells with an amount effective of the laminin 8 to promote cell adhesion to the surface.

28. An improved cell growth substrate, wherein the improvement consists of providing a cell growth substrate that has been coated with an amount effective of laminin 8 to promote cell attachment to the cell growth substrate.

29. The method of any of claims 18-28, wherein the laminin 8 comprises recombinant laminin 8.

30. A method to accelerate healing of a vascular tissue injury in a subject, comprising contacting the site of the vascular tissue injury of the subject with an amount effective of the pharmaceutical composition of claim 16 or 17 to promote re-endothelialization at the vascular tissue injury site.

31. The method of claim 30, wherein the vascular injury is selected from the group consisting of angioplasty restenosis, vascular surgical procedures, aneurysm, and atherosclerosis

32. A method to accelerate healing of a bone or connective tissue injury in a subject comprising contacting the site of the bone or connective tissue injury in the subject with an amount effective of the pharmaceutical composition of claim 16 or 17 to accelerate healing of the bone or connective tissue injury.

33. The method of claim 32 wherein healing is accomplished by incorporation of recombinant laminin 8 into wound repair dressings, matrices, or tissue grafts.

34. The method of claim 32 wherein the bone or connective tissue injury is selected from the group consisting of fractures, tears, deformities, or defects of bone, tendon, cartilage, and ligament.

35. A method to improve the biocompatibility of a medical device or graft, comprising contacting the medical device or graft with an amount effective of the pharmaceutical composition of claim 16 or 17 to improve the biocompatibility of the medical device or graft.

36. An improved medical device or graft, wherein the improvement consists of providing a medical device or graft with an amount effective of the pharmaceutical composition of claim 16 or 17 to improve the biocompatibility of the medical device or graft.

37. A method to promote angiogenesis in a subject, comprising contacting a site in need of angiogenesis in the subject with an amount effective of the pharmaceutical composition of claim 16 or 17 to promote angiogenesis.

38. A method to promote neural regeneration in a subject, comprising contacting a site in need of neural regeneration in the subject with an amount effective of the pharmaceutical composition of claim 16 or 17 to promote neural regeneration.

39. A method to promote cell adhesion to a surface, comprising contacting cells with an amount effective of the pharmaceutical composition of claim 16 or 17 to promote cell adhesion to the surface.

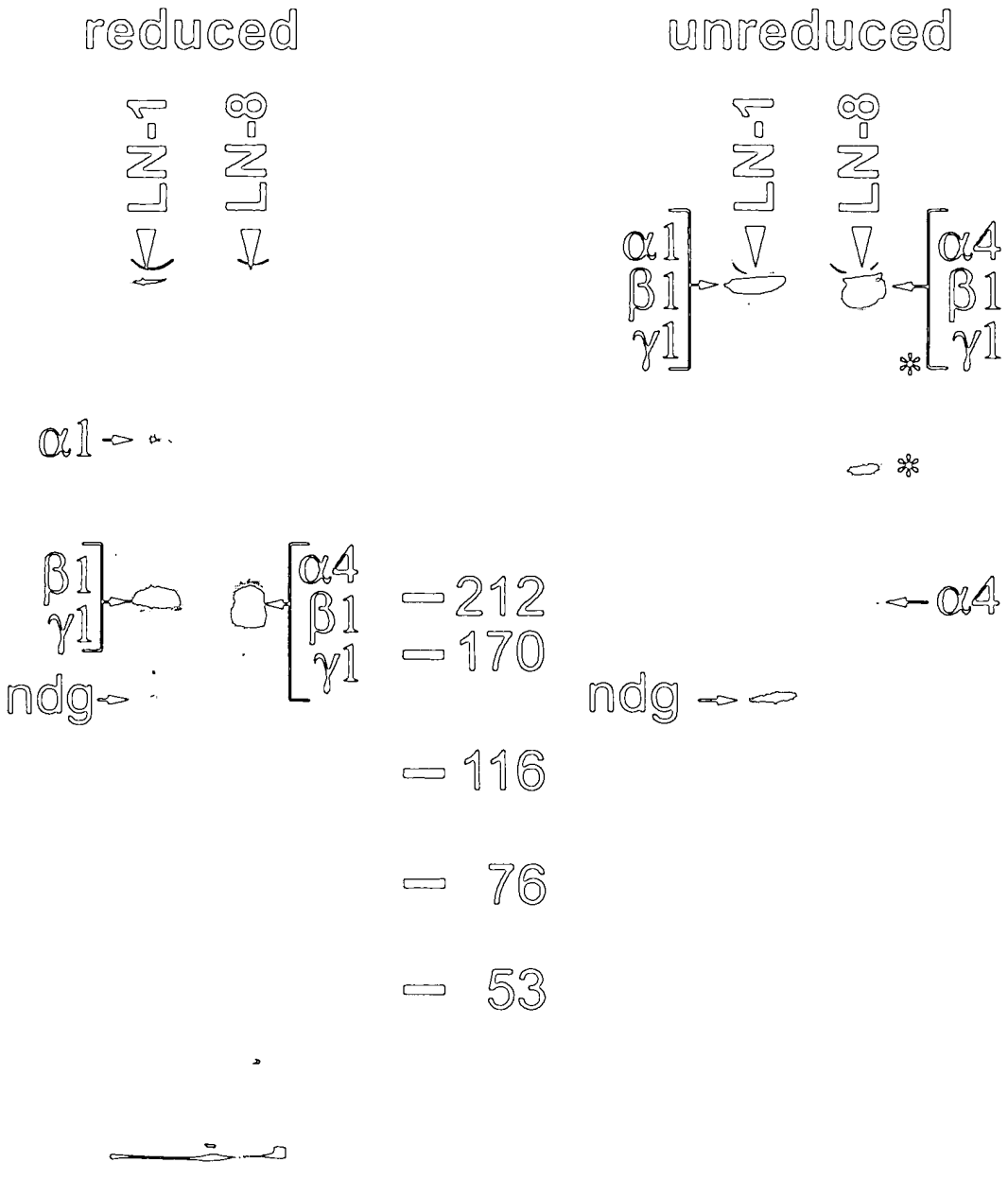
40. An improved cell growth substrate, wherein the improvement consists of providing a cell growth substrate that has been coated with an amount effective of the pharmaceutical composition of claim 16 or 17 to promote cell attachment to the cell growth substrate.

41. A kit for carrying out the method of any of claims 18-28, comprising:

(a) an amount effective of laminin 8 for carrying out the method; and

(b) instructions for using the laminin 8 for carrying out the method.

42. A method to inhibit cell adhesion to laminin 8, comprising contacting the cell with an amount effective of an antagonist of at least one of integrin $\alpha 6\beta 1$ and $\alpha 6\beta 4$ to inhibit cell adhesion to laminin 8.


reduced
unreduced
LN-1
LN-8
α1
β1
γ1
α4
β1
γ1
*
α1
β1
γ1
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γ1
ndg
ndg
α4
212
170
116
76
53

FIG. 1

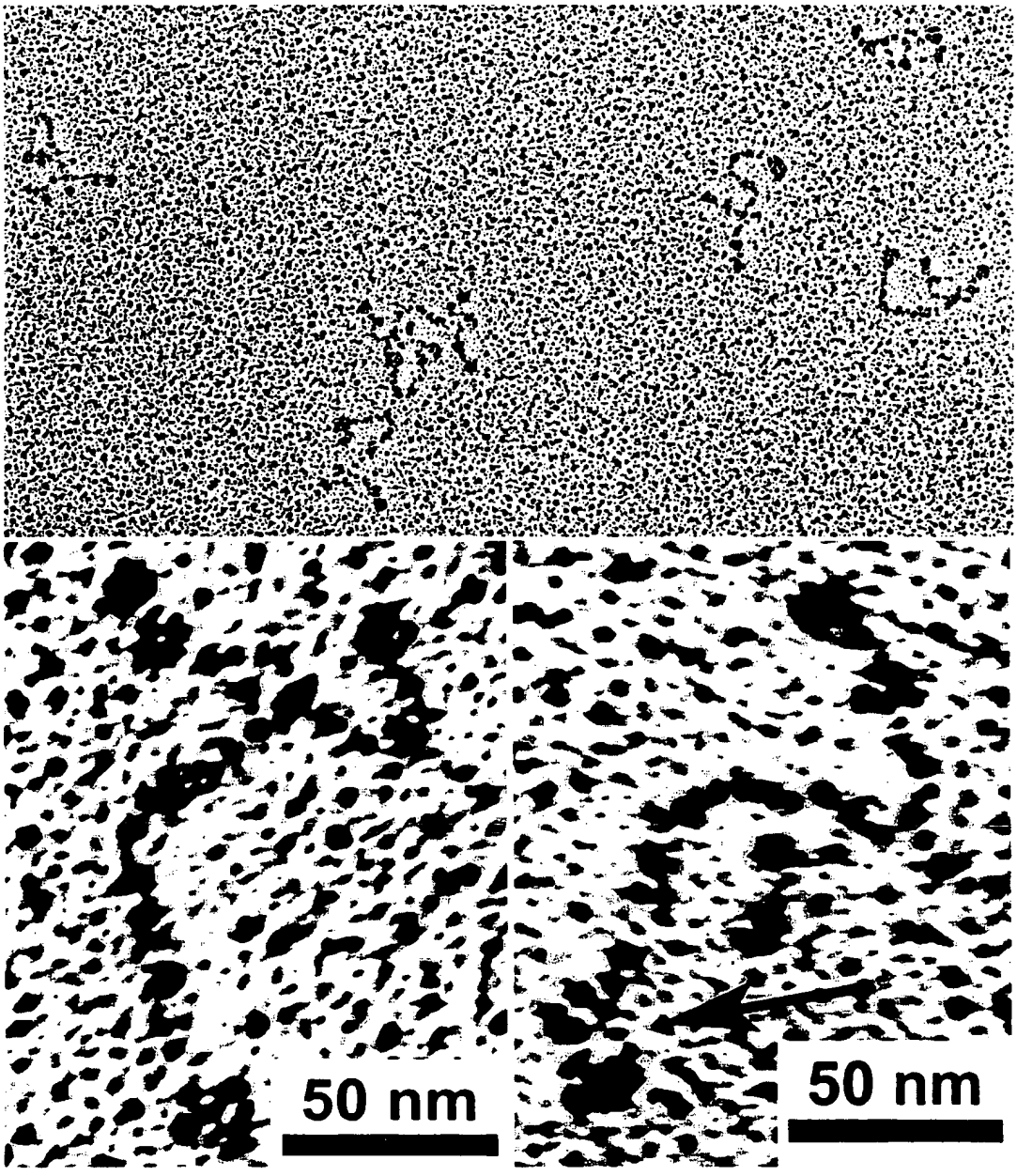


FIG. 2

FIG. 3

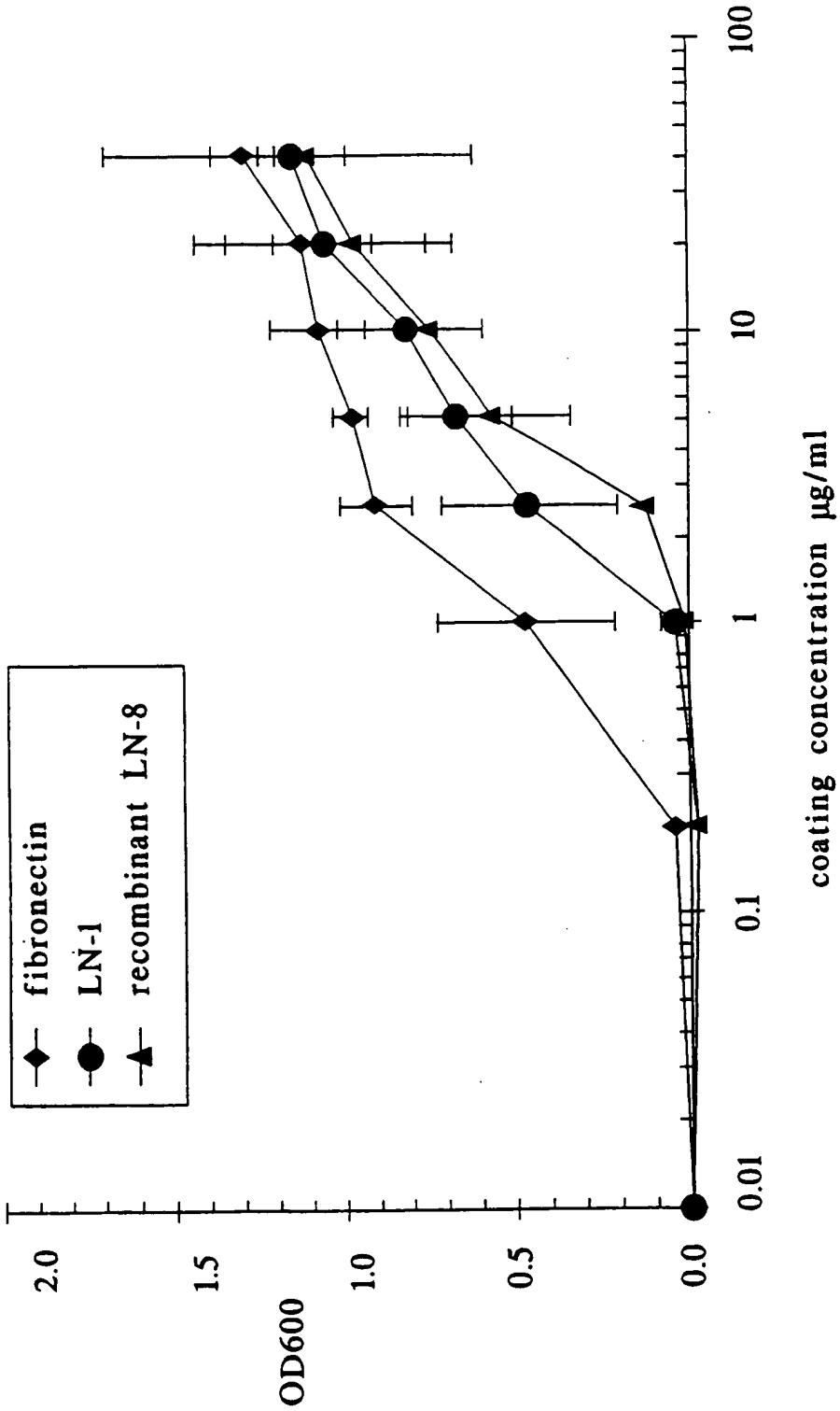

fibronectin
LN-1
recombinant LN-8
OD600
2.0
1.5
1.0
0.5
0.0
0.01
0.1
1
10
100
coating concentration µg/ml

FIG. 4

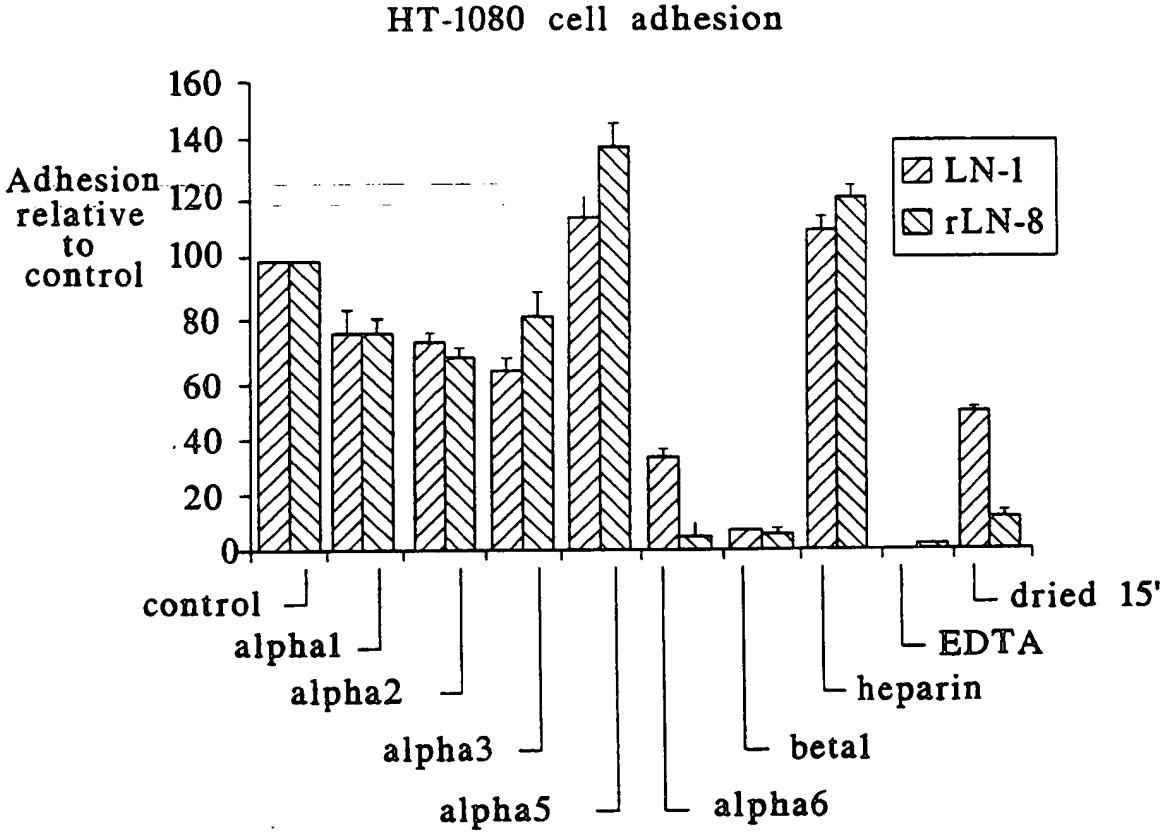

HT-1080 cell adhesion
Adhesion relative to control
160
140
120
100
80
60
40
20
0
LN-1
rLN-8
control
alpha1
alpha2
alpha3
alpha5
alpha6
beta1
heparin
EDTA
dried 15'

FIG. 5

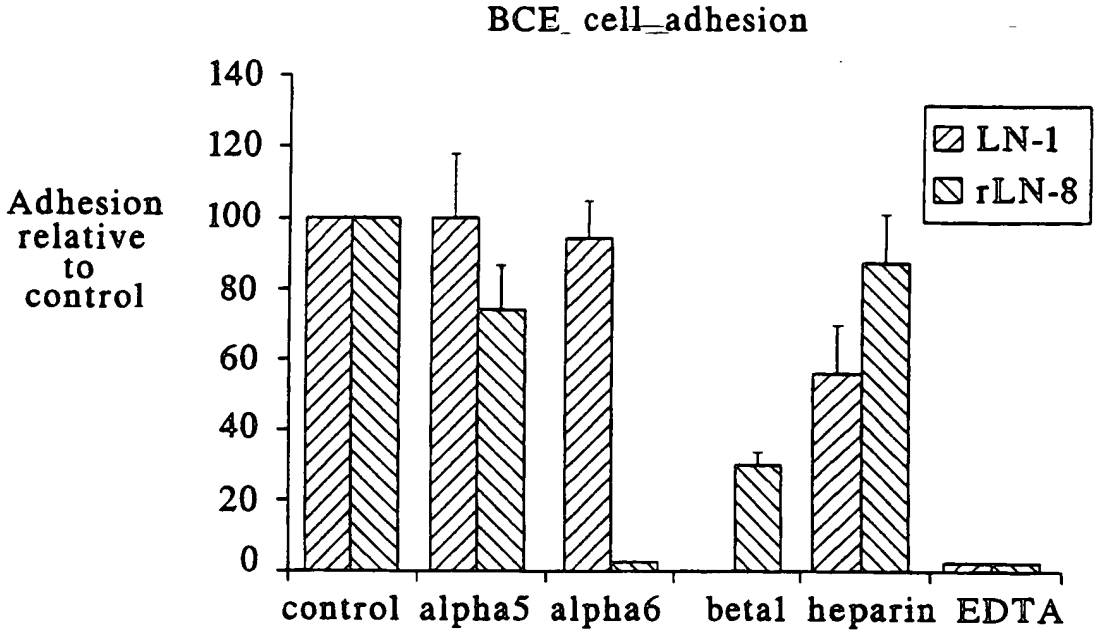
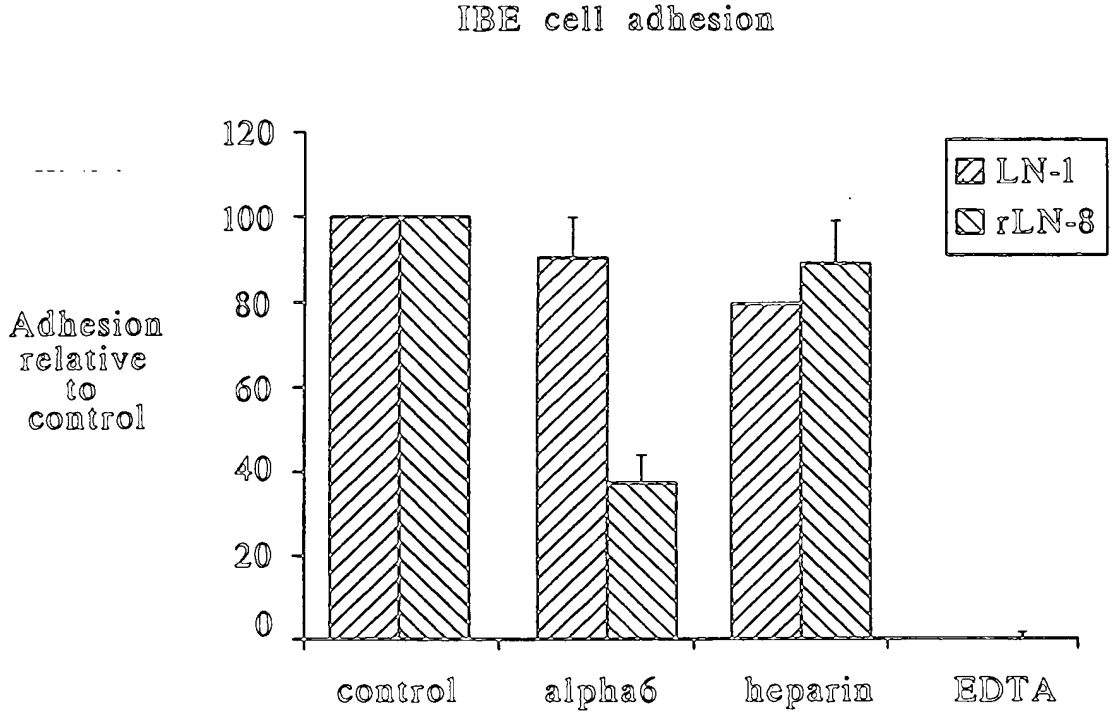

BCE_ cell_adhesion
Adhesion relative to control
140
120
100
80
60
40
20
0
LN-1
rLN-8
control
alpha5
alpha6
betal
heparin
EDTA

FIG. 6


IBE cell adhesion
Adhesion relative to control
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100
80
60
40
20
0
LN-1
rLN-8
control
alpha6
heparin
EDTA

FIG. 7

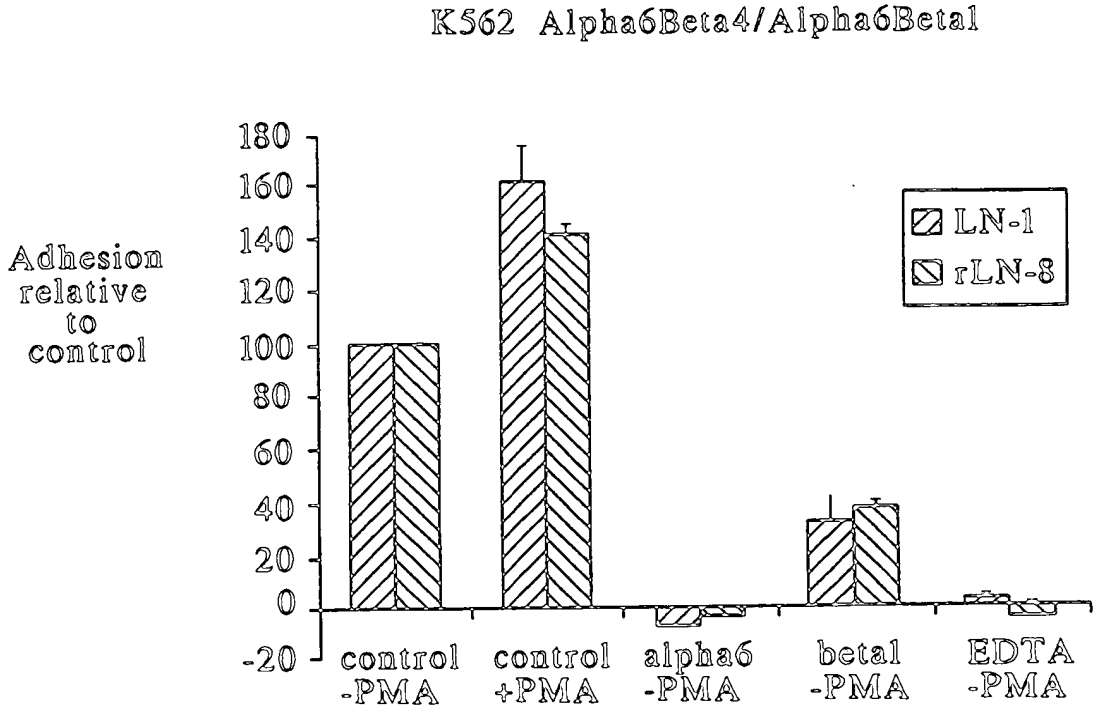
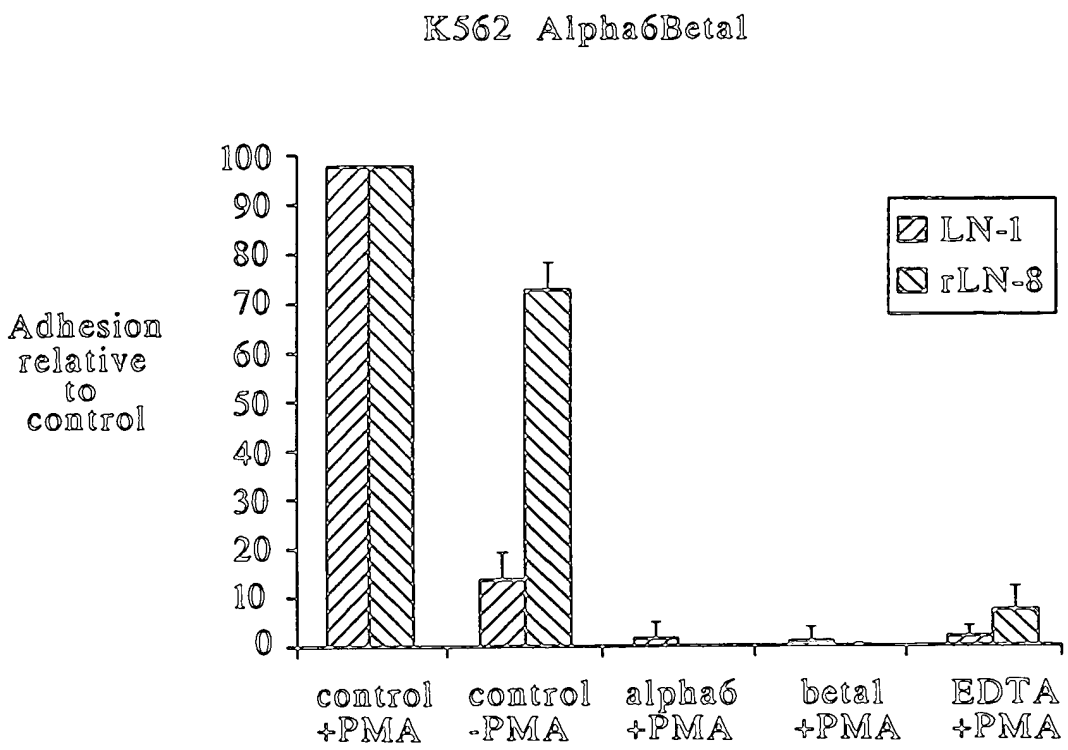

K562 Alpha6Beta4/Alpha6Beta1
Adhesion relative to control
180
160
140
120
100
80
60
40
20
0
-20
LN-1
rLN-8
control -PMA
control +PMA
alpha6 -PMA
beta1 -PMA
EDTA -PMA

FIG. 8


K562 Alpha6Beta1
Adhesion relative to control
100
90
80
70
60
50
40
30
20
10
0
LN-1
rLN-8
control +PMA
control -PMA
alpha6 +PMA
beta1 +PMA
EDTA +PMA

SEQUENCE LISTING

<110> Kortesmaa, Jarrko
Tryggvason, Karl

<120> Laminin 8 and Methods For Its Use

<130> 99,274-D1

<140> To Be Assigned
<141> Filed Herewith

<160> 28

<170> PatentIn Ver. 2.0

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ccacgcggag acctacggag acccacagcg cccgagccct ggaagagcac tactggatgt 180

cagcggagaa atg gct ttg agc tca gcc tgg cgc tcg gtt ctg cct ctg 229
Met Ala Leu Ser Ser Ala Trp Arg Ser Val Leu Pro Leu
1 5 10

tgg ctc ctc tgg agc gct gcc tgc tcc cgc gcc gcg tcc ggg gac gac 277
Trp Leu Leu Trp Ser Ala Ala Cys Ser Arg Ala Ala Ser Gly Asp Asp
15 20 25

aac gct ttt cct ttt gac att gaa ggg agc tca gcg gtt ggc agg caa 325
Asn Ala Phe Pro Phe Asp Ile Glu Gly Ser Ser Ala Val Gly Arg Gln
30 35 40 45

gac ccg cct gag acg agc gaa ccc cgc gtg gct ctg gga cgc ctg ccg 373
Asp Pro Pro Glu Thr Ser Glu Pro Arg Val Ala Leu Gly Arg Leu Pro
50 55 60

cct gcg gcc gag aaa tgc aat gct gga ttc ttt cac acc ctg tcg gga 421
Pro Ala Ala Glu Lys Cys Asn Ala Gly Phe Phe His Thr Leu Ser Gly
65 70 75

gaa tgt gtg ccc tgc gac tgt aat ggc aat tcc aac gag tgt ttg gac 469
Glu Cys Val Pro Cys Asp Cys Asn Gly Asn Ser Asn Glu Cys Leu Asp
80 85 90

ggc tca gga tac tgt gtg cac tgc cag cgg aac aca aca gga gag cac 517

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Gly Ser Gly Tyr Cys Val His Cys Gln Arg Asn Thr Thr Gly Glu His
     95                  100                 105

tgt gaa aag tgt ctg gat ggt tat atc gga gat tcc atc agg gga gca   565
Cys Glu Lys Cys Leu Asp Gly Tyr Ile Gly Asp Ser Ile Arg Gly Ala
110                 115                 120                 125

ccc caa ttc tgc cag ccg tgc ccc tgt ccc ctg ccc cac ttg gcc aat   613
Pro Gln Phe Cys Gln Pro Cys Pro Cys Pro Leu Pro His Leu Ala Asn
                130                 135                 140

ttt cca gaa tcc tgc tat agg aaa aat gga gct gtt cgg tgc att tgt   661
Phe Pro Glu Ser Cys Tyr Arg Lys Asn Gly Ala Val Arg Cys Ile Cys
            145                 150                 155

aac gaa aat tat gct gga cct aac tgt gaa aga tgt gct ccc ggt tac   709
Asn Glu Asn Tyr Ala Gly Pro Asn Cys Glu Arg Cys Ala Pro Gly Tyr
        160                 165                 170

tat gga aac ccc ttc ctc att gga agc acc tgt aag aaa tgt gac tgc   757
Tyr Gly Asn Pro Phe Leu Ile Gly Ser Thr Cys Lys Lys Cys Asp Cys
    175                 180                 185

agt gga aat tca gat ccc aac ctg atc ttt gaa gat tgt gat gaa gtc   805
Ser Gly Asn Ser Asp Pro Asn Leu Ile Phe Glu Asp Cys Asp Glu Val
190                 195                 200                 205

act ggc cag tgt agg aat tgc tta cgc aac acc acc gga ttc aag tgt   853
Thr Gly Gln Cys Arg Asn Cys Leu Arg Asn Thr Thr Gly Phe Lys Cys
                210                 215                 220

gaa cgt tgc gct cct ggc tac tat ggg gac gcc agg ata gcc aag aac   901
Glu Arg Cys Ala Pro Gly Tyr Tyr Gly Asp Ala Arg Ile Ala Lys Asn
            225                 230                 235

tgt gca gtg tgc aac tgc ggg gga ggc cca tgt gac agt gta acc gga   949
Cys Ala Val Cys Asn Cys Gly Gly Gly Pro Cys Asp Ser Val Thr Gly
        240                 245                 250

gaa tgc ttg gaa gaa ggt ttt gaa ccc cct aca ggc tgt gat aag tgc   997
Glu Cys Leu Glu Glu Gly Phe Glu Pro Pro Thr Gly Cys Asp Lys Cys
    255                 260                 265

gtc tgg gac ctg act gat gac ctg cgg tta gca gcg ctc tcc atc gag  1045
Val Trp Asp Leu Thr Asp Asp Leu Arg Leu Ala Ala Leu Ser Ile Glu
270                 275                 280                 285

gaa ggc aaa tcc ggg gtg ctg agc gta tcc tct ggg gcc gcc gct cat  1093
Glu Gly Lys Ser Gly Val Leu Ser Val Ser Ser Gly Ala Ala Ala His
                290                 295                 300

agg cac gtg aat gaa atc aac gcc acc atc tac ctc ctc aaa aca aaa  1141
Arg His Val Asn Glu Ile Asn Ala Thr Ile Tyr Leu Leu Lys Thr Lys
            305                 310                 315

ttg tca gaa aga gaa aac caa tac gcc cta aga aag ata caa atc aac  1189
Leu Ser Glu Arg Glu Asn Gln Tyr Ala Leu Arg Lys Ile Gln Ile Asn
        320                 325                 330

aat gct gag aac acg atg aaa agc ctt ctg tct gac gta gag gaa tta  1237
Asn Ala Glu Asn Thr Met Lys Ser Leu Leu Ser Asp Val Glu Glu Leu
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350                 355                 360                 365

gaa agc atg gac acc att aac cac gca agt cag ctg gta gag caa gcc   1333
Glu Ser Met Asp Thr Ile Asn His Ala Ser Gln Leu Val Glu Gln Ala
                370                 375                 380

cat gat atg agg gat aaa atc caa gag atc aac aac aag atg ctc tat   1381
His Asp Met Arg Asp Lys Ile Gln Glu Ile Asn Asn Lys Met Leu Tyr
            385                 390                 395

tat ggg gaa gag cat gaa ctt agc ccc aag gaa atc tct gag aag ctg   1429
Tyr Gly Glu Glu His Glu Leu Ser Pro Lys Glu Ile Ser Glu Lys Leu
        400                 405                 410

gtg ttg gcc cag aag atg ctt gaa gag att aga agc cgt caa cca ttt   1477
Val Leu Ala Gln Lys Met Leu Glu Glu Ile Arg Ser Arg Gln Pro Phe
    415                 420                 425

ttc acc caa cgg gag ctc gtg gat gag gag gca gat gag gct tac gaa   1525
Phe Thr Gln Arg Glu Leu Val Asp Glu Glu Ala Asp Glu Ala Tyr Glu
430                 435                 440                 445

cta ctg agc cag gct gag agc tgg cag cgg ctg cac aat gag acc cgc   1573
Leu Leu Ser Gln Ala Glu Ser Trp Gln Arg Leu His Asn Glu Thr Arg
                450                 455                 460

act ctg ttt cct gtc gtc ctg gag cag ctg gat gac tac aat gct aag   1621
Thr Leu Phe Pro Val Val Leu Glu Gln Leu Asp Asp Tyr Asn Ala Lys
            465                 470                 475

ttg tca gat ctc cag gaa gca ctt gac cag gcc ctt aac tat gtc agg   1669
Leu Ser Asp Leu Gln Glu Ala Leu Asp Gln Ala Leu Asn Tyr Val Arg
        480                 485                 490

gat gcc gaa gac atg aac agg gcc aca gca gcc agg cag cgg gac cat   1717
Asp Ala Glu Asp Met Asn Arg Ala Thr Ala Ala Arg Gln Arg Asp His
    495                 500                 505

gag aaa caa cag gaa aga gtg agg gaa caa atg gaa gtg gtg aac atg   1765
Glu Lys Gln Gln Glu Arg Val Arg Glu Gln Met Glu Val Val Asn Met
510                 515                 520                 525

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Ser Leu Ser Thr Ser Ala Asp Ser Leu Thr Thr Pro Arg Leu Thr Leu
                530                 535                 540

tca gaa ctt gat gat ata ata aag aat gcg tca ggg att tat gca gaa   1861
Ser Glu Leu Asp Asp Ile Ile Lys Asn Ala Ser Gly Ile Tyr Ala Glu
            545                 550                 555

ata gat gga gcc aaa agt gaa cta caa gta aaa cta tct aac cta agt   1909
Ile Asp Gly Ala Lys Ser Glu Leu Gln Val Lys Leu Ser Asn Leu Ser
        560                 565                 570

aac ctc agc cat gat tta gtc caa gaa gct att gac cat gca cag gac   1957
Asn Leu Ser His Asp Leu Val Gln Glu Ala Ile Asp His Ala Gln Asp
    575                 580                 585
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590                 595                 600                 605

atg aac ggg ctg gta cag aag gct ttg gat gca tca aat gtc tat gaa   2053
Met Asn Gly Leu Val Gln Lys Ala Leu Asp Ala Ser Asn Val Tyr Glu
                610                 615                 620

aat att gtt aat tat gtt agt gaa gcc aat gaa aca gca gaa ttt gct   2101
Asn Ile Val Asn Tyr Val Ser Glu Ala Asn Glu Thr Ala Glu Phe Ala
            625                 630                 635

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Leu Asn Thr Thr Asp Arg Ile Tyr Asp Ala Val Ser Gly Ile Asp Thr
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Gln Ile Ile Tyr His Lys Asp Glu Ser Glu Asn Leu Leu Asn Gln Ala
    655                 660                 665

aga gaa ctg caa gca aag gca gag tct agc agt gat gaa gca gtg gct   2245
Arg Glu Leu Gln Ala Lys Ala Glu Ser Ser Ser Asp Glu Ala Val Ala
670                 675                 680                 685

gac act agc agg cgt gtg ggt gga gcc cta gca agg aaa agt gcc ctt   2293
Asp Thr Ser Arg Arg Val Gly Gly Ala Leu Ala Arg Lys Ser Ala Leu
                690                 695                 700

aaa acc aga ctc agt gat gcc gtt aag caa cta caa gca gca gag aga   2341
Lys Thr Arg Leu Ser Asp Ala Val Lys Gln Leu Gln Ala Ala Glu Arg
            705                 710                 715

ggg gat gcc cag cag cgc ctg ggg cag tct aga ctg atc acc gag gaa   2389
Gly Asp Ala Gln Gln Arg Leu Gly Gln Ser Arg Leu Ile Thr Glu Glu
        720                 725                 730

gcc aac agg acg acg atg gag gtg cag cag gcc act gcc ccc atg gcc   2437
Ala Asn Arg Thr Thr Met Glu Val Gln Gln Ala Thr Ala Pro Met Ala
    735                 740                 745

aac aat cta acc aac tgg tca cag aat ctt caa cat ttt gac tct tct   2485
Asn Asn Leu Thr Asn Trp Ser Gln Asn Leu Gln His Phe Asp Ser Ser
750                 755                 760                 765

gct tac aac act gca gtg aac tct gct agg gat gca gta aga aat ctg   2533
Ala Tyr Asn Thr Ala Val Asn Ser Ala Arg Asp Ala Val Arg Asn Leu
                770                 775                 780

acc gag gtt gtc cct cag ctc ctg gat cag ctt cgt acg gtt gag cag   2581
Thr Glu Val Val Pro Gln Leu Leu Asp Gln Leu Arg Thr Val Glu Gln
            785                 790                 795

aag cga cct gca agc aac gtt tct gcc agc atc cag agg atc cga gag   2629
Lys Arg Pro Ala Ser Asn Val Ser Ala Ser Il  Gln Arg Ile Arg Glu
        800                 805                 810

ctc att gct cag acc aga agt gtt gcc agc aag atc caa gtc tcc atg   2677
Leu Ile Ala Gln Thr Arg Ser Val Ala Ser Lys Ile Gln Val Ser Met
    815                 820                 825
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atg ttt gat ggc cag tca gct gtg gaa gtg cac tcg aga acc agt atg   2725
Met Phe Asp Gly Gln Ser Ala Val Glu Val His Ser Arg Thr Ser Met
830                 835                 840                 845

gat gac tta aag gcc ttc acg tct ctg agc ctg tac atg aaa ccc cct   2773
Asp Asp Leu Lys Ala Phe Thr Ser Leu Ser Leu Tyr Met Lys Pro Pro
                850                 855                 860

gtg aag cgg ccg gaa ctg acc gag act gca gat cag ttt atc ctg tac   2821
Val Lys Arg Pro Glu Leu Thr Glu Thr Ala Asp Gln Phe Ile Leu Tyr
            865                 870                 875

ctc gga agc aaa aac gcc aaa aaa gag tat atg ggt ctt gca atc aaa   2869
Leu Gly Ser Lys Asn Ala Lys Lys Glu Tyr Met Gly Leu Ala Ile Lys
        880                 885                 890

aat gat aat ctg gta tac gtc tat aat ttg gga act aaa gat gtg gag   2917
Asn Asp Asn Leu Val Tyr Val Tyr Asn Leu Gly Thr Lys Asp Val Glu
    895                 900                 905

att ccc ctg gac tcc aag ccc gtc agt tcc tgg cct gct tac ttc agc   2965
Ile Pro Leu Asp Ser Lys Pro Val Ser Ser Trp Pro Ala Tyr Phe Ser
910                 915                 920                 925

att gtc aag att gaa agg gtg gga aaa cat gga aag gtg ttt tta aca   3013
Ile Val Lys Ile Glu Arg Val Gly Lys His Gly Lys Val Phe Leu Thr
                930                 935                 940

gtc ccg agt cta agt agc aca gca gag gaa aag ttc att aaa aag ggg   3061
Val Pro Ser Leu Ser Ser Thr Ala Glu Glu Lys Phe Ile Lys Lys Gly
            945                 950                 955

gaa ttt tcg gga gat gac tct ctg ctg gac ctg gac cct gag gac aca   3109
Glu Phe Ser Gly Asp Asp Ser Leu Leu Asp Leu Asp Pro Glu Asp Thr
        960                 965                 970

gtg ttt tat gtt ggt gga gtg cct tcc aac ttc aag ctc cct acc agc   3157
Val Phe Tyr Val Gly Gly Val Pro Ser Asn Phe Lys Leu Pro Thr Ser
    975                 980                 985

tta aac ctg cct ggc ttt gtt ggc tgc ctg gaa ctg gcc act ttg aat   3205
Leu Asn Leu Pro Gly Phe Val Gly Cys Leu Glu Leu Ala Thr Leu Asn
990                 995                1000                1005

aat gat gtg atc agc ttg tac aac ttt aag cac atc tat aat atg gac   3253
Asn Asp Val Ile Ser Leu Tyr Asn Phe Lys His Ile Tyr Asn Met Asp
                1010                1015                1020

ccc tcc aca tca gtg cca tgt gcc cga gat aag ctg gcc ttc act cag   3301
Pro Ser Thr Ser Val Pro Cys Ala Arg Asp Lys Leu Ala Phe Thr Gln
            1025                1030                1035

agt cgg gct gcc agt tac ttc ttc gat ggc tcc ggt tat gcc gtg gtg   3349
Ser Arg Ala Ala Ser Tyr Phe Phe Asp Gly Ser Gly Tyr Ala Val Val
        1040                1045                1050

aga gac ata cca agg aga ggg aaa ttt ggt cag gtg act cgc ttt gac   3397
Arg Asp Ile Pro Arg Arg Gly Lys Phe Gly Gln Val Thr Arg Phe Asp
    1055                1060                1065

ata gaa gtt cga aca cca gct gac aac ggc ctt att ctc ctg atg gtc   3445
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Ile Glu Val Arg Thr Pro Ala Asp Asn Gly Leu Ile Leu Leu Met Val
1070                1075                1080                1085

aat gga agt atg ttt ttc aga ctg gaa atg cgc aat ggt tac cta cat   3493
Asn Gly Ser Met Phe Phe Arg Leu Glu Met Arg Asn Gly Tyr Leu His
                1090                1095                1100

gtg ttc tat gat ttt gga ttc agc agt ggc cgt gtg cat ctt gaa gat   3541
Val Phe Tyr Asp Phe Gly Phe Ser Ser Gly Arg Val His Leu Glu Asp
            1105                1110                1115

acg tta aag aaa gct caa att aat gat gca aaa tac cat gag atc tca   3589
Thr Leu Lys Lys Ala Gln Ile Asn Asp Ala Lys Tyr His Glu Ile Ser
        1120                1125                1130

atc att tac cac aat gat aag aaa atg atc ttg gta gtt gac aga agg   3637
Ile Ile Tyr His Asn Asp Lys Lys Met Ile Leu Val Val Asp Arg Arg
    1135                1140                1145

cat gtc aag agc atg gat aat gaa aag atg aaa ata cct ttt aca gat   3685
His Val Lys Ser Met Asp Asn Glu Lys Met Lys Ile Pro Phe Thr Asp
1150                1155                1160                1165

ata tac att gga gga gct cct cca gaa atc tta caa tcc agg gcc ctc   3733
Ile Tyr Ile Gly Gly Ala Pro Pro Glu Ile Leu Gln Ser Arg Ala Leu
                1170                1175                1180

aga gca cac ctt ccc cta gat atc aac ttc aga gga tgc atg aag ggc   3781
Arg Ala His Leu Pro Leu Asp Ile Asn Phe Arg Gly Cys Met Lys Gly
            1185                1190                1195

ttc cag ttc caa aag aag gac ttc aat tta ctg gag cag aca gaa acc   3829
Phe Gln Phe Gln Lys Lys Asp Phe Asn Leu Leu Glu Gln Thr Glu Thr
        1200                1205                1210

ctg gga gtt ggt tat gga tgc cca gaa gac tca ctt ata tct cgc aga   3877
Leu Gly Val Gly Tyr Gly Cys Pro Glu Asp Ser Leu Ile Ser Arg Arg
    1215                1220                1225

gca tat ttc aat gga cag agc ttc att gct tca att cag aaa ata tct   3925
Ala Tyr Phe Asn Gly Gln Ser Phe Ile Ala Ser Ile Gln Lys Ile Ser
1230                1235                1240                1245

ttc ttt gat ggc ttt gaa gga ggt ttt aat ttc cga aca tta caa cca   3973
Phe Phe Asp Gly Phe Glu Gly Gly Phe Asn Phe Arg Thr Leu Gln Pro
                1250                1255                1260

aat ggg tta cta ttc tat tat gct tca ggg tca gac gtg ttc tcc atc   4021
Asn Gly Leu Leu Phe Tyr Tyr Ala Ser Gly Ser Asp Val Phe Ser Ile
            1265                1270                1275

tca ctg gat aat ggt act gtc atc atg gat gta aag gga atc aaa gtt   4069
Ser Leu Asp Asn Gly Thr Val Ile Met Asp Val Lys Gly Ile Lys Val
        1280                1285                1290

cag tca gta gat aag cag tac aat gat ggg ctg tcc cac ttc gtc att   4117
Gln Ser Val Asp Lys Gln Tyr Asn Asp Gly Leu Ser His Phe Val Ile
    1295                1300                1305

agc tct gtc tca ccc aca aga tat gaa ctg ata gta gat aaa agc aga   4165
Ser Ser Val Ser Pro Thr Arg Tyr Glu Leu Ile Val Asp Lys Ser Arg
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1310                1315                1320                1325

gtt ggg agt aag aat cct acc aaa ggg aaa ata gaa cag aca caa gca   4213
Val Gly Ser Lys Asn Pro Thr Lys Gly Lys Ile Glu Gln Thr Gln Ala
                1330                1335                1340

agt gaa aag aag ttt tac ttc ggt ggc tca cca atc agt gct cag tat   4261
Ser Glu Lys Lys Phe Tyr Phe Gly Gly Ser Pro Ile Ser Ala Gln Tyr
            1345                1350                1355

gct aat ttc act ggc tgc ata agt aat gcc tac ttt acc agg gtg gat   4309
Ala Asn Phe Thr Gly Cys Ile Ser Asn Ala Tyr Phe Thr Arg Val Asp
        1360                1365                1370

aga gat gtg gag gtt gaa gat ttc caa cgg tat act gaa aag gtc cac   4357
Arg Asp Val Glu Val Glu Asp Phe Gln Arg Tyr Thr Glu Lys Val His
    1375                1380                1385

act tct ctt tat gag tgt ccc att gag tct tca cca ttg ttt ctc ctc   4405
Thr Ser Leu Tyr Glu Cys Pro Ile Glu Ser Ser Pro Leu Phe Leu Leu
1390                1395                1400                1405

cat aaa aaa gga aaa aat tta tcc aag cct aaa gca agt cag aat aaa   4453
His Lys Lys Gly Lys Asn Leu Ser Lys Pro Lys Ala Ser Gln Asn Lys
                1410                1415                1420

aag gga ggg aaa agt aaa gat gca cct tca tgg gat cct gtt gct ctg   4501
Lys Gly Gly Lys Ser Lys Asp Ala Pro Ser Trp Asp Pro Val Ala Leu
            1425                1430                1435

aaa ctc cca gag cgg aat act cca aga aac tct cat tgc cac ctt tcc   4549
Lys Leu Pro Glu Arg Asn Thr Pro Arg Asn Ser His Cys His Leu Ser
        1440                1445                1450

aac agc cct aga gca ata gag cac gcc tat caa tat gga gga aca gcc   4597
Asn Ser Pro Arg Ala Ile Glu His Ala Tyr Gln Tyr Gly Gly Thr Ala
    1455                1460                1465

aac agc cgc caa gag ttt gaa cac tta aaa gga gat ttt ggt gcc aaa   4645
Asn Ser Arg Gln Glu Phe Glu His Leu Lys Gly Asp Phe Gly Ala Lys
1470                1475                1480                1485

tct cag ttt tcc att cgt ctg aga act cgt tcc tcc cat ggc atg atc   4693
Ser Gln Phe Ser Ile Arg Leu Arg Thr Arg Ser Ser His Gly Met Ile
                1490                1495                1500

ttc tat gtc tca gat caa gaa gag aat gac ttc atg act cta ttt ttg   4741
Phe Tyr Val Ser Asp Gln Glu Glu Asn Asp Phe Met Thr Leu Phe Leu
            1505                1510                1515

gcc cat ggc cgc ttg gtt tac atg ttt aat gtt ggt cac aaa aaa ctg   4789
Ala His Gly Arg Leu Val Tyr Met Phe Asn Val Gly His Lys Lys Leu
        1520                1525                1530

aag att aga agc cag gag aaa tac aat gat ggc ctg tgg cat gat gtg   4837
Lys Ile Arg Ser Gln Glu Lys Tyr Asn Asp Gly Leu Trp His Asp Val
    1535                1540                1545

ata ttt att cga gaa agg agc agt ggc cga ctg gta att gat ggt ctc   4885
Ile Phe Ile Arg Glu Arg Ser Ser Gly Arg Leu Val Ile Asp Gly Leu
1550                1555                1560                1565
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cga gtc cta gaa gaa agt ctt cct cct act gaa gct acc tgg aaa atc   4933
Arg Val Leu Glu Glu Ser Leu Pro Pro Thr Glu Ala Thr Trp Lys Ile
                1570                1575                1580

aag ggt ccc att tat ttg gga ggt gtg gct cct gga aag gct gtg aaa   4981
Lys Gly Pro Ile Tyr Leu Gly Gly Val Ala Pro Gly Lys Ala Val Lys
            1585                1590                1595

aat gtt cag att aac tcc atc tac agt ttt agt ggc tgt ctc agc aat   5029
Asn Val Gln Ile Asn Ser Ile Tyr Ser Phe Ser Gly Cys Leu Ser Asn
        1600                1605                1610

ctc cag ctc aat ggg gcc tcc atc acc tct gct tct cag aca ttc agt   5077
Leu Gln Leu Asn Gly Ala Ser Ile Thr Ser Ala Ser Gln Thr Phe Ser
    1615                1620                1625

gtg acc cct tgc ttt gaa ggc ccc atg gaa aca gga act tac ttt tca   5125
Val Thr Pro Cys Phe Glu Gly Pro Met Glu Thr Gly Thr Tyr Phe Ser
1630                1635                1640                1645

aca gaa gga gga tac gtg gtt cta gat gaa tct ttc aat att gga ttg   5173
Thr Glu Gly Gly Tyr Val Val Leu Asp Glu Ser Phe Asn Ile Gly Leu
                1650                1655                1660

aag ttt gaa att gca ttt gaa gtc cgt ccc aga agc agt tcc gga acc   5221
Lys Phe Glu Ile Ala Phe Glu Val Arg Pro Arg Ser Ser Ser Gly Thr
            1665                1670                1675

ctg gtc cac ggc cac agt gtc aat ggg gag tac cta aat gtt cac atg   5269
Leu Val His Gly His Ser Val Asn Gly Glu Tyr Leu Asn Val His Met
        1680                1685                1690

aaa aat gga cag gtc ata gtg aaa gtc aat aat ggc atc aga gat ttt   5317
Lys Asn Gly Gln Val Ile Val Lys Val Asn Asn Gly Ile Arg Asp Phe
    1695                1700                1705

tcc acc tca gta aca ccc aag cag agt ctc tgt gat ggc aga tgg cac   5365
Ser Thr Ser Val Thr Pro Lys Gln Ser Leu Cys Asp Gly Arg Trp His
1710                1715                1720                1725

aga att aca gtt att aga gat tct aat gtg gtt cag ttg gat gtg gac   5413
Arg Ile Thr Val Ile Arg Asp Ser Asn Val Val Gln Leu Asp Val Asp
                1730                1735                1740

tct gaa gtg aac cat gtg gtt gga ccc ctg aat cca aaa cca att gat   5461
Ser Glu Val Asn His Val Val Gly Pro Leu Asn Pro Lys Pro Ile Asp
            1745                1750                1755

cac agg gag cct gtg ttt gtt gga ggt gtt cca gaa tct cta ctg aca   5509
His Arg Glu Pro Val Phe Val Gly Gly Val Pro Glu Ser Leu Leu Thr
        1760                1765                1770

cca cgc ttg gcc ccc agc aaa ccc ttc aca ggc tgc ata cgc cac ttt   5557
Pro Arg Leu Ala Pro Ser Lys Pro Phe Thr Gly Cys Ile Arg His Phe
    1775                1780                1785

gtg att gat gga cac cca gtg agc ttc agt aaa gca gcc ctg gtc agc   5605
Val Ile Asp Gly His Pro Val Ser Phe Ser Lys Ala Ala Leu Val Ser
1790                1795                1800                1805
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ggc gcc gta agc atc aac tcc tgt cca gca gcc tgacatgaca gagcacagct 5658
Gly Ala Val Ser Ile Asn Ser Cys Pro Ala Ala
               1810                1815

gcccaaatac aaagttcttt agagcactga aagaaacaca aagccagcca ggaggaacag 5718

taactcttcc ttcgggtgga agctttcatc gagttgaaca ggacttaaac gaatcatcag 5778

ggaccggata tttcttattt ctcatttgga ttcttaacct tgaatccaaa gtgtctgcaa 5838

tggacaacaa ttgaaggaga ggcaaactta cttgtattga gagcacacgc aattcctact 5898

ggtgaaatta ctgtttctgt ttctaataaa atagaaggga ttccaaataa acacttgcac 5958

acatttttga agtgcggcta gattctcaga ttcacctttc ttccagggaa gataactttc 6018

aatctatata aaaatctctg tcctaaaact acctttcttt attttgaaga gacttactaa 6078

cttacatata atctaaatta gatgatagat ttctttttag ccctttttgtt tggtctatca 6138

gtataagaag aatattttag gtttatagct gaagttatca aggtttaata aagtaaattt 6198

ctaaca                                                          6204
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<210> 2
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Met Ala Leu Ser Ser Ala Trp Arg Ser Val Leu Pro Leu Trp Leu Leu
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Trp Ser Ala Ala Cys Ser Arg Ala Ala Ser Gly Asp Asp Asn Ala Phe
            20                  25                  30

Pro Phe Asp Ile Glu Gly Ser Ser Ala Val Gly Arg Gln Asp Pro Pro
         35                  40                  45

Glu Thr Ser Glu Pro Arg Val Ala Leu Gly Arg Leu Pro Pro Ala Ala
     50                  55                  60

Glu Lys Cys Asn Ala Gly Phe Phe His Thr Leu Ser Gly Glu Cys Val
 65                  70                  75                  80

Pro Cys Asp Cys Asn Gly Asn Ser Asn Glu Cys Leu Asp Gly Ser Gly
                 85                  90                  95

Tyr Cys Val His Cys Gln Arg Asn Thr Thr Gly Glu His Cys Glu Lys
            100                 105                 110

Cys Leu Asp Gly Tyr Ile Gly Asp Ser Ile Arg Gly Ala Pro Gln Phe
        115                 120                 125

Cys Gln Pro Cys Pro Cys Pro Leu Pro His Leu Ala Asn Phe Pro Glu
    130                 135                 140

Ser Cys Tyr Arg Lys Asn Gly Ala Val Arg Cys Ile Cys Asn Glu Asn
145                 150                 155                 160
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Tyr Ala Gly Pro Asn Cys Glu Arg Cys Ala Pro Gly Tyr Tyr Gly Asn
                165                 170                 175

Pro Phe Leu Ile Gly Ser Thr Cys Lys Lys Cys Asp Cys Ser Gly Asn
            180                 185                 190

Ser Asp Pro Asn Leu Ile Phe Glu Asp Cys Asp Glu Val Thr Gly Gln
        195                 200                 205

Cys Arg Asn Cys Leu Arg Asn Thr Thr Gly Phe Lys Cys Glu Arg Cys
    210                 215                 220

Ala Pro Gly Tyr Tyr Gly Asp Ala Arg Ile Ala Lys Asn Cys Ala Val
225                 230                 235                 240

Cys Asn Cys Gly Gly Gly Pro Cys Asp Ser Val Thr Gly Glu Cys Leu
                245                 250                 255

Glu Glu Gly Phe Glu Pro Pro Thr Gly Cys Asp Lys Cys Val Trp Asp
            260                 265                 270

Leu Thr Asp Asp Leu Arg Leu Ala Ala Leu Ser Ile Glu Glu Gly Lys
        275                 280                 285

Ser Gly Val Leu Ser Val Ser Ser Gly Ala Ala Ala His Arg His Val
    290                 295                 300

Asn Glu Ile Asn Ala Thr Ile Tyr Leu Leu Lys Thr Lys Leu Ser Glu
305                 310                 315                 320

Arg Glu Asn Gln Tyr Ala Leu Arg Lys Ile Gln Ile Asn Asn Ala Glu
                325                 330                 335

Asn Thr Met Lys Ser Leu Leu Ser Asp Val Glu Glu Leu Val Glu Lys
            340                 345                 350

Glu Asn Gln Ala Ser Arg Lys Gly Gln Leu Val Gln Lys Glu Ser Met
        355                 360                 365

Asp Thr Ile Asn His Ala Ser Gln Leu Val Glu Gln Ala His Asp Met
    370                 375                 380

Arg Asp Lys Ile Gln Glu Ile Asn Asn Lys Met Leu Tyr Tyr Gly Glu
385                 390                 395                 400

Glu His Glu Leu Ser Pro Lys Glu Ile Ser Glu Lys Leu Val Leu Ala
                405                 410                 415

Gln Lys Met Leu Glu Glu Ile Arg Ser Arg Gln Pro Phe Phe Thr Gln
            420                 425                 430

Arg Glu Leu Val Asp Glu Glu Ala Asp Glu Ala Tyr Glu Leu Leu Ser
        435                 440                 445

Gln Ala Glu Ser Trp Gln Arg Leu His Asn Glu Thr Arg Thr Leu Phe
    450                 455                 460

Pro Val Val Leu Glu Gln Leu Asp Asp Tyr Asn Ala Lys Leu Ser Asp
465                 470                 475                 480

Leu Gln Glu Ala Leu Asp Gln Ala Leu Asn Tyr Val Arg Asp Ala Glu
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485 490 495

Asp Met Asn Arg Ala Thr Ala Ala Arg Gln Arg Asp His Glu Lys Gln
500 505 510

Gln Glu Arg Val Arg Glu Gln Met Glu Val Val Asn Met Ser Leu Ser
515 520 525

Thr Ser Ala Asp Ser Leu Thr Thr Pro Arg Leu Thr Leu Ser Glu Leu
530 535 540

Asp Asp Ile Ile Lys Asn Ala Ser Gly Ile Tyr Ala Glu Ile Asp Gly
545 550 555 560

Ala Lys Ser Glu Leu Gln Val Lys Leu Ser Asn Leu Ser Asn Leu Ser
565 570 575

His Asp Leu Val Gln Glu Ala Ile Asp His Ala Gln Asp Leu Gln Gln
580 585 590

Glu Ala Asn Glu Leu Ser Arg Lys Leu His Ser Ser Asp Met Asn Gly
595 600 605

Leu Val Gln Lys Ala Leu Asp Ala Ser Asn Val Tyr Glu Asn Ile Val
610 615 620

Asn Tyr Val Ser Glu Ala Asn Glu Thr Ala Glu Phe Ala Leu Asn Thr
625 630 635 640

Thr Asp Arg Ile Tyr Asp Ala Val Ser Gly Ile Asp Thr Gln Ile Ile
645 650 655

Tyr His Lys Asp Glu Ser Glu Asn Leu Leu Asn Gln Ala Arg Glu Leu
660 665 670

Gln Ala Lys Ala Glu Ser Ser Ser Asp Glu Ala Val Ala Asp Thr Ser
675 680 685

Arg Arg Val Gly Gly Ala Leu Ala Arg Lys Ser Ala Leu Lys Thr Arg
690 695 700

Leu Ser Asp Ala Val Lys Gln Leu Gln Ala Ala Glu Arg Gly Asp Ala
705 710 715 720

Gln Gln Arg Leu Gly Gln Ser Arg Leu Ile Thr Glu Glu Ala Asn Arg
725 730 735

Thr Thr Met Glu Val Gln Gln Ala Thr Ala Pro Met Ala Asn Asn Leu
740 745 750

Thr Asn Trp Ser Gln Asn Leu Gln His Phe Asp Ser Ser Ala Tyr Asn
755 760 765

Thr Ala Val Asn Ser Ala Arg Asp Ala Val Arg Asn Leu Thr Glu Val
770 775 780

Val Pro Gln Leu Leu Asp Gln Leu Arg Thr Val Glu Gln Lys Arg Pro
785 790 795 800

Ala Ser Asn Val Ser Ala Ser Ile Gln Arg Ile Arg Glu Leu Ile Ala
805 810 815

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Gln Thr Arg Ser Val Ala Ser Lys Ile Gln Val Ser Met Met Phe Asp
            820                 825                 830

Gly Gln Ser Ala Val Glu Val His Ser Arg Thr Ser Met Asp Asp Leu
        835                 840                 845

Lys Ala Phe Thr Ser Leu Ser Leu Tyr Met Lys Pro Pro Val Lys Arg
    850                 855                 860

Pro Glu Leu Thr Glu Thr Ala Asp Gln Phe Ile Leu Tyr Leu Gly Ser
865                 870                 875                 880

Lys Asn Ala Lys Lys Glu Tyr Met Gly Leu Ala Ile Lys Asn Asp Asn
                885                 890                 895

Leu Val Tyr Val Tyr Asn Leu Gly Thr Lys Asp Val Glu Ile Pro Leu
            900                 905                 910

Asp Ser Lys Pro Val Ser Ser Trp Pro Ala Tyr Phe Ser Ile Val Lys
        915                 920                 925

Ile Glu Arg Val Gly Lys His Gly Lys Val Phe Leu Thr Val Pro Ser
    930                 935                 940

Leu Ser Ser Thr Ala Glu Glu Lys Phe Ile Lys Lys Gly Glu Phe Ser
945                 950                 955                 960

Gly Asp Asp Ser Leu Leu Asp Leu Asp Pro Glu Asp Thr Val Phe Tyr
                965                 970                 975

Val Gly Gly Val Pro Ser Asn Phe Lys Leu Pro Thr Ser Leu Asn Leu
            980                 985                 990

Pro Gly Phe Val Gly Cys Leu Glu Leu Ala Thr Leu Asn Asn Asp Val
        995                1000                1005

Ile Ser Leu Tyr Asn Phe Lys His Ile Tyr Asn Met Asp Pro Ser Thr
   1010                1015                1020

Ser Val Pro Cys Ala Arg Asp Lys Leu Ala Phe Thr Gln Ser Arg Ala
025                1030                1035                1040

Ala Ser Tyr Phe Phe Asp Gly Ser Gly Tyr Ala Val Val Arg Asp Ile
               1045                1050                1055

Pro Arg Arg Gly Lys Phe Gly Gln Val Thr Arg Phe Asp Ile Glu Val
           1060                1065                1070

Arg Thr Pro Ala Asp Asn Gly Leu Ile Leu Leu Met Val Asn Gly Ser
       1075                1080                1085

Met Phe Phe Arg Leu Glu Met Arg Asn Gly Tyr Leu His Val Phe Tyr
   1090                1095                1100

Asp Phe Gly Phe Ser Ser Gly Arg Val His Leu Glu Asp Thr Leu Lys
105                1110                1115                1120

Lys Ala Gln Ile Asn Asp Ala Lys Tyr His Glu Ile Ser Ile Ile Tyr
               1125                1130                1135
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His Asn Asp Lys Lys Met Ile Leu Val Val Asp Arg Arg His Val Lys
          1140                1145                1150

Ser Met Asp Asn Glu Lys Met Lys Ile Pro Phe Thr Asp Ile Tyr Ile
       1155                1160                1165

Gly Gly Ala Pro Pro Glu Ile Leu Gln Ser Arg Ala Leu Arg Ala His
   1170                1175                1180

Leu Pro Leu Asp Ile Asn Phe Arg Gly Cys Met Lys Gly Phe Gln Phe
185                1190                1195                1200

Gln Lys Lys Asp Phe Asn Leu Leu Glu Gln Thr Glu Thr Leu Gly Val
               1205                1210                1215

Gly Tyr Gly Cys Pro Glu Asp Ser Leu Ile Ser Arg Arg Ala Tyr Phe
          1220                1225                1230

Asn Gly Gln Ser Phe Ile Ala Ser Ile Gln Lys Ile Ser Phe Phe Asp
       1235                1240                1245

Gly Phe Glu Gly Gly Phe Asn Phe Arg Thr Leu Gln Pro Asn Gly Leu
   1250                1255                1260

Leu Phe Tyr Tyr Ala Ser Gly Ser Asp Val Phe Ser Ile Ser Leu Asp
265                1270                1275                1280

Asn Gly Thr Val Ile Met Asp Val Lys Gly Ile Lys Val Gln Ser Val
               1285                1290                1295

Asp Lys Gln Tyr Asn Asp Gly Leu Ser His Phe Val Ile Ser Ser Val
          1300                1305                1310

Ser Pro Thr Arg Tyr Glu Leu Ile Val Asp Lys Ser Arg Val Gly Ser
       1315                1320                1325

Lys Asn Pro Thr Lys Gly Lys Ile Glu Gln Thr Gln Ala Ser Glu Lys
   1330                1335                1340

Lys Phe Tyr Phe Gly Gly Ser Pro Ile Ser Ala Gln Tyr Ala Asn Phe
345                1350                1355                1360

Thr Gly Cys Ile Ser Asn Ala Tyr Phe Thr Arg Val Asp Arg Asp Val
               1365                1370                1375

Glu Val Glu Asp Phe Gln Arg Tyr Thr Glu Lys Val His Thr Ser Leu
          1380                1385                1390

Tyr Glu Cys Pro Ile Glu Ser Ser Pro Leu Phe Leu Leu His Lys Lys
       1395                1400                1405

Gly Lys Asn Leu Ser Lys Pro Lys Ala Ser Gln Asn Lys Lys Gly Gly
   1410                1415                1420

Lys Ser Lys Asp Ala Pro Ser Trp Asp Pro Val Ala Leu Lys Leu Pro
425                1430                1435                1440

Glu Arg Asn Thr Pro Arg Asn Ser His Cys His Leu Ser Asn Ser Pro
               1445                1450                1455

Arg Ala Ile Glu His Ala Tyr Gln Tyr Gly Gly Thr Ala Asn Ser Arg
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Gln Glu Phe Glu His Leu Lys Gly Asp Phe Gly Ala Lys Ser Gln Phe
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Ser Ile Arg Leu Arg Thr Arg Ser Ser His Gly Met Ile Phe Tyr Val
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Ser Asp Gln Glu Glu Asn Asp Phe Met Thr Leu Phe Leu Ala His Gly
505 1510 1515 1520

Arg Leu Val Tyr Met Phe Asn Val Gly His Lys Lys Leu Lys Ile Arg
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Ser Gln Glu Lys Tyr Asn Asp Gly Leu Trp His Asp Val Ile Phe Ile
1540 1545 1550

Arg Glu Arg Ser Ser Gly Arg Leu Val Ile Asp Gly Leu Arg Val Leu
1555 1560 1565

Glu Glu Ser Leu Pro Pro Thr Glu Ala Thr Trp Lys Ile Lys Gly Pro
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Ile Tyr Leu Gly Gly Val Ala Pro Gly Lys Ala Val Lys Asn Val Gln
585 1590 1595 1600

Ile Asn Ser Ile Tyr Ser Phe Ser Gly Cys Leu Ser Asn Leu Gln Leu
1605 1610 1615

Asn Gly Ala Ser Ile Thr Ser Ala Ser Gln Thr Phe Ser Val Thr Pro
1620 1625 1630

Cys Phe Glu Gly Pro Met Glu Thr Gly Thr Tyr Phe Ser Thr Glu Gly
1635 1640 1645

Gly Tyr Val Val Leu Asp Glu Ser Phe Asn Ile Gly Leu Lys Phe Glu
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Ile Ala Phe Glu Val Arg Pro Arg Ser Ser Ser Gly Thr Leu Val His
665 1670 1675 1680

Gly His Ser Val Asn Gly Glu Tyr Leu Asn Val His Met Lys Asn Gly
1685 1690 1695

Gln Val Ile Val Lys Val Asn Asn Gly Ile Arg Asp Phe Ser Thr Ser
1700 1705 1710

Val Thr Pro Lys Gln Ser Leu Cys Asp Gly Arg Trp His Arg Ile Thr
1715 1720 1725

Val Ile Arg Asp Ser Asn Val Val Gln Leu Asp Val Asp Ser Glu Val
1730 1735 1740

Asn His Val Val Gly Pro Leu Asn Pro Lys Pro Ile Asp His Arg Glu
745 1750 1755 1760

Pro Val Phe Val Gly Gly Val Pro Glu Ser Leu Leu Thr Pro Arg Leu
1765 1770 1775

Ala Pro Ser Lys Pro Phe Thr Gly Cys Ile Arg His Phe Val Ile Asp
1780 1785 1790

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Ser Ile Asn Ser Cys Pro Ala Ala
   1810                1815


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gcg gtt ggc agg caa gac ccg cct gag acg agc gaa ccc cgc gtg gct   96
Ala Val Gly Arg Gln Asp Pro Pro Glu Thr Ser Glu Pro Arg Val Ala
             20                  25                  30

ctg gga cgc ctg ccg cct gcg gcc gag aaa tgc aat gct gga ttc ttt   144
Leu Gly Arg Leu Pro Pro Ala Ala Glu Lys Cys Asn Ala Gly Phe Phe
         35                  40                  45

cac acc ctg tcg gga gaa tgt gtg ccc tgc gac tgt aat ggc aat tcc   192
His Thr Leu Ser Gly Glu Cys Val Pro Cys Asp Cys Asn Gly Asn Ser
     50                  55                  60

aac gag tgt ttg gac ggc tca gga tac tgt gtg cac tgc cag cgg aac   240
Asn Glu Cys Leu Asp Gly Ser Gly Tyr Cys Val His Cys Gln Arg Asn
 65                  70                  75                  80

aca aca gga gag cac tgt gaa aag tgt ctg gat ggt tat atc gga gat   288
Thr Thr Gly Glu His Cys Glu Lys Cys Leu Asp Gly Tyr Ile Gly Asp
                 85                  90                  95

tcc atc agg gga gca ccc caa ttc tgc cag ccg tgc ccc tgt ccc ctg   336
Ser Ile Arg Gly Ala Pro Gln Phe Cys Gln Pro Cys Pro Cys Pro Leu
            100                 105                 110

ccc cac ttg gcc aat ttt cca gaa tcc tgc tat agg aaa aat gga gct   384
Pro His Leu Ala Asn Phe Pro Glu Ser Cys Tyr Arg Lys Asn Gly Ala
        115                 120                 125

gtt cgg tgc att tgt aac gaa aat tat gct gga cct aac tgt gaa aga   432
Val Arg Cys Ile Cys Asn Glu Asn Tyr Ala Gly Pro Asn Cys Glu Arg
    130                 135                 140

tgt gct ccc ggt tac tat gga aac ccc ttc ctc att gga agc acc tgt   480
Cys Ala Pro Gly Tyr Tyr Gly Asn Pro Phe Leu Ile Gly Ser Thr Cys
145                 150                 155                 160

aag aaa tgt gac tgc agt gga aat tca gat ccc aac ctg atc ttt gaa   528
Lys Lys Cys Asp Cys Ser Gly Asn Ser Asp Pro Asn Leu Ile Phe Glu
                165                 170                 175
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gat tgt gat gaa gtc act ggc cag tgt agg aat tgc tta cgc aac acc   576
Asp Cys Asp Glu Val Thr Gly Gln Cys Arg Asn Cys Leu Arg Asn Thr
            180                 185                 190

acc gga ttc aag tgt gaa cgt tgc gct cct ggc tac tat ggg gac gcc   624
Thr Gly Phe Lys Cys Glu Arg Cys Ala Pro Gly Tyr Tyr Gly Asp Ala
        195                 200                 205

agg ata gcc aag aac tgt gca gtg tgc aac tgc ggg gga ggc cca tgt   672
Arg Ile Ala Lys Asn Cys Ala Val Cys Asn Cys Gly Gly Gly Pro Cys
    210                 215                 220

gac agt gta acc gga gaa tgc ttg gaa gaa ggt ttt gaa ccc cct aca   720
Asp Ser Val Thr Gly Glu Cys Leu Glu Glu Gly Phe Glu Pro Pro Thr
225                 230                 235                 240

ggc tgt gat aag tgc gtc tgg gac ctg act gat gac ctg cgg tta gca   768
Gly Cys Asp Lys Cys Val Trp Asp Leu Thr Asp Asp Leu Arg Leu Ala
                245                 250                 255

gcg ctc tcc atc gag gaa ggc aaa tcc ggg gtg ctg agc gta tcc tct   816
Ala Leu Ser Ile Glu Glu Gly Lys Ser Gly Val Leu Ser Val Ser Ser
            260                 265                 270

ggg gcc gcc gct cat agg cac gtg aat gaa atc aac gcc acc atc tac   864
Gly Ala Ala Ala His Arg His Val Asn Glu Ile Asn Ala Thr Ile Tyr
        275                 280                 285

ctc ctc aaa aca aaa ttg tca gaa aga gaa aac caa tac gcc cta aga   912
Leu Leu Lys Thr Lys Leu Ser Glu Arg Glu Asn Gln Tyr Ala Leu Arg
    290                 295                 300

aag ata caa atc aac aat gct gag aac acg atg aaa agc ctt ctg tct   960
Lys Ile Gln Ile Asn Asn Ala Glu Asn Thr Met Lys Ser Leu Leu Ser
305                 310                 315                 320

gac gta gag gaa tta gtt gaa aag gaa aat caa gcc tcc aga aaa gga  1008
Asp Val Glu Glu Leu Val Glu Lys Glu Asn Gln Ala Ser Arg Lys Gly
                325                 330                 335

caa ctt gtt cag aag gaa agc atg gac acc att aac cac gca agt cag  1056
Gln Leu Val Gln Lys Glu Ser Met Asp Thr Ile Asn His Ala Ser Gln
            340                 345                 350

ctg gta gag caa gcc cat gat atg agg gat aaa atc caa gag atc aac  1104
Leu Val Glu Gln Ala His Asp Met Arg Asp Lys Ile Gln Glu Ile Asn
        355                 360                 365

aac aag atg ctc tat tat ggg gaa gag cat gaa ctt agc ccc aag gaa  1152
Asn Lys Met Leu Tyr Tyr Gly Glu Glu His Glu Leu Ser Pro Lys Glu
    370                 375                 380

atc tct gag aag ctg gtg ttg gcc cag aag atg ctt gaa gag att aga  1200
Ile Ser Glu Lys Leu Val Leu Ala Gln Lys Met Leu Glu Glu Ile Arg
385                 390                 395                 400

agc cgt caa cca ttt ttc acc caa cgg gag ctc gtg gat gag gag gca  1248
Ser Arg Gln Pro Phe Phe Thr Gln Arg Glu Leu Val Asp Glu Glu Ala
                405                 410                 415
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gat gag gct tac gaa cta ctg agc cag gct gag agc tgg cag cgg ctg   1296
Asp Glu Ala Tyr Glu Leu Leu Ser Gln Ala Glu Ser Trp Gln Arg Leu
            420                 425                 430

cac aat gag acc cgc act ctg ttt cct gtc gtc ctg gag cag ctg gat   1344
His Asn Glu Thr Arg Thr Leu Phe Pro Val Val Leu Glu Gln Leu Asp
        435                 440                 445

gac tac aat gct aag ttg tca gat ctc cag gaa gca ctt gac cag gcc   1392
Asp Tyr Asn Ala Lys Leu Ser Asp Leu Gln Glu Ala Leu Asp Gln Ala
    450                 455                 460

ctt aac tat gtc agg gat gcc gaa gac atg aac agg gcc aca gca gcc   1440
Leu Asn Tyr Val Arg Asp Ala Glu Asp Met Asn Arg Ala Thr Ala Ala
465                 470                 475                 480

agg cag cgg gac cat gag aaa caa cag gaa aga gtg agg gaa caa atg   1488
Arg Gln Arg Asp His Glu Lys Gln Gln Glu Arg Val Arg Glu Gln Met
                485                 490                 495

gaa gtg gtg aac atg tct ctg agc aca tct gcg gac tct ctg aca aca   1536
Glu Val Val Asn Met Ser Leu Ser Thr Ser Ala Asp Ser Leu Thr Thr
            500                 505                 510

cct cgt cta act ctt tca gaa ctt gat gat ata ata aag aat gcg tca   1584
Pro Arg Leu Thr Leu Ser Glu Leu Asp Asp Ile Ile Lys Asn Ala Ser
        515                 520                 525

ggg att tat gca gaa ata gat gga gcc aaa agt gaa cta caa gta aaa   1632
Gly Ile Tyr Ala Glu Ile Asp Gly Ala Lys Ser Glu Leu Gln Val Lys
    530                 535                 540

cta tct aac cta agt aac ctc agc cat gat tta gtc caa gaa gct att   1680
Leu Ser Asn Leu Ser Asn Leu Ser His Asp Leu Val Gln Glu Ala Ile
545                 550                 555                 560

gac cat gca cag gac ctt caa caa gaa gct aat gaa ttg agc agg aag   1728
Asp His Ala Gln Asp Leu Gln Gln Glu Ala Asn Glu Leu Ser Arg Lys
                565                 570                 575

ttg cac agt tca gat atg aac ggg ctg gta cag aag gct ttg gat gca   1776
Leu His Ser Ser Asp Met Asn Gly Leu Val Gln Lys Ala Leu Asp Ala
            580                 585                 590

tca aat gtc tat gaa aat att gtt aat tat gtt agt gaa gcc aat gaa   1824
Ser Asn Val Tyr Glu Asn Ile Val Asn Tyr Val Ser Glu Ala Asn Glu
        595                 600                 605

aca gca gaa ttt gct ttg aac acc act gac cga att tat gat gcg gtg   1872
Thr Ala Glu Phe Ala Leu Asn Thr Thr Asp Arg Ile Tyr Asp Ala Val
    610                 615                 620

agt ggg att gat act caa atc att tac cat aaa gat gaa agt gag aac   1920
Ser Gly Ile Asp Thr Gln Ile Ile Tyr His Lys Asp Glu Ser Glu Asn
625                 630                 635                 640

ctc ctc aat caa gcc aga gaa ctg caa gca aag gca gag tct agc agt   1968
Leu Leu Asn Gln Ala Arg Glu Leu Gln Ala Lys Ala Glu Ser Ser Ser
                645                 650                 655

gat gaa gca gtg gct gac act agc agg cgt gtg ggt gga gcc cta gca   2016
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Asp Glu Ala Val Ala Asp Thr Ser Arg Arg Val Gly Gly Ala Leu Ala
            660                 665                 670

agg aaa agt gcc ctt aaa acc aga ctc agt gat gcc gtt aag caa cta   2064
Arg Lys Ser Ala Leu Lys Thr Arg Leu Ser Asp Ala Val Lys Gln Leu
        675                 680                 685

caa gca gca gag aga ggg gat gcc cag cag cgc ctg ggg cag tct aga   2112
Gln Ala Ala Glu Arg Gly Asp Ala Gln Gln Arg Leu Gly Gln Ser Arg
    690                 695                 700

ctg atc acc gag gaa gcc aac agg acg acg atg gag gtg cag cag gcc   2160
Leu Ile Thr Glu Glu Ala Asn Arg Thr Thr Met Glu Val Gln Gln Ala
705                 710                 715                 720

act gcc ccc atg gcc aac aat cta acc aac tgg tca cag aat ctt caa   2208
Thr Ala Pro Met Ala Asn Asn Leu Thr Asn Trp Ser Gln Asn Leu Gln
                725                 730                 735

cat ttt gac tct tct gct tac aac act gca gtg aac tct gct agg gat   2256
His Phe Asp Ser Ser Ala Tyr Asn Thr Ala Val Asn Ser Ala Arg Asp
            740                 745                 750

gca gta aga aat ctg acc gag gtt gtc cct cag ctc ctg gat cag ctt   2304
Ala Val Arg Asn Leu Thr Glu Val Val Pro Gln Leu Leu Asp Gln Leu
        755                 760                 765

cgt acg gtt gag cag aag cga cct gca agc aac gtt tct gcc agc atc   2352
Arg Thr Val Glu Gln Lys Arg Pro Ala Ser Asn Val Ser Ala Ser Ile
    770                 775                 780

cag agg atc cga gag ctc att gct cag acc aga agt gtt gcc agc aag   2400
Gln Arg Ile Arg Glu Leu Ile Ala Gln Thr Arg Ser Val Ala Ser Lys
785                 790                 795                 800

atc caa gtc tcc atg atg ttt gat ggc cag tca gct gtg gaa gtg cac   2448
Ile Gln Val Ser Met Met Phe Asp Gly Gln Ser Ala Val Glu Val His
                805                 810                 815

tcg aga acc agt atg gat gac tta aag gcc ttc acg tct ctg agc ctg   2496
Ser Arg Thr Ser Met Asp Asp Leu Lys Ala Phe Thr Ser Leu Ser Leu
            820                 825                 830

tac atg aaa ccc cct gtg aag cgg ccg gaa ctg acc gag act gca gat   2544
Tyr Met Lys Pro Pro Val Lys Arg Pro Glu Leu Thr Glu Thr Ala Asp
        835                 840                 845

cag ttt atc ctg tac ctc gga agc aaa aac gcc aaa aaa gag tat atg   2592
Gln Phe Ile Leu Tyr Leu Gly Ser Lys Asn Ala Lys Lys Glu Tyr Met
    850                 855                 860

ggt ctt gca atc aaa aat gat aat ctg gta tac gtc tat aat ttg gga   2640
Gly Leu Ala Ile Lys Asn Asp Asn Leu Val Tyr Val Tyr Asn Leu Gly
865                 870                 875                 880

act aaa gat gtg gag att ccc ctg gac tcc aag ccc gtc agt tcc tgg   2688
Thr Lys Asp Val Glu Ile Pro Leu Asp Ser Lys Pro Val Ser Ser Trp
                885                 890                 895

cct gct tac ttc agc att gtc aag att gaa agg gtg gga aaa cat gga   2736
Pro Ala Tyr Phe Ser Ile Val Lys Ile Glu Arg Val Gly Lys His Gly
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            900                 905                 910

aag gtg ttt tta aca gtc ccg agt cta agt agc aca gca gag gaa aag   2784
Lys Val Phe Leu Thr Val Pro Ser Leu Ser Ser Thr Ala Glu Glu Lys
        915                 920                 925

ttc att aaa aag ggg gaa ttt tcg gga gat gac tct ctg ctg gac ctg   2832
Phe Ile Lys Lys Gly Glu Phe Ser Gly Asp Asp Ser Leu Leu Asp Leu
    930                 935                 940

gac cct gag gac aca gtg ttt tat gtt ggt gga gtg cct tcc aac ttc   2880
Asp Pro Glu Asp Thr Val Phe Tyr Val Gly Gly Val Pro Ser Asn Phe
945                 950                 955                 960

aag ctc cct acc agc tta aac ctg cct ggc ttt gtt ggc tgc ctg gaa   2928
Lys Leu Pro Thr Ser Leu Asn Leu Pro Gly Phe Val Gly Cys Leu Glu
                965                 970                 975

ctg gcc act ttg aat aat gat gtg atc agc ttg tac aac ttt aag cac   2976
Leu Ala Thr Leu Asn Asn Asp Val Ile Ser Leu Tyr Asn Phe Lys His
            980                 985                 990

atc tat aat atg gac ccc tcc aca tca gtg cca tgt gcc cga gat aag   3024
Ile Tyr Asn Met Asp Pro Ser Thr Ser Val Pro Cys Ala Arg Asp Lys
        995                1000                1005

ctg gcc ttc act cag agt cgg gct gcc agt tac ttc ttc gat ggc tcc   3072
Leu Ala Phe Thr Gln Ser Arg Ala Ala Ser Tyr Phe Phe Asp Gly Ser
   1010                1015                1020

ggt tat gcc gtg gtg aga gac ata cca agg aga ggg aaa ttt ggt cag   3120
Gly Tyr Ala Val Val Arg Asp Ile Pro Arg Arg Gly Lys Phe Gly Gln
1025                1030                1035                1040

gtg act cgc ttt gac ata gaa gtt cga aca cca gct gac aac ggc ctt   3168
Val Thr Arg Phe Asp Ile Glu Val Arg Thr Pro Ala Asp Asn Gly Leu
                1045                1050                1055

att ctc ctg atg gtc aat gga agt atg ttt ttc aga ctg gaa atg cgc   3216
Ile Leu Leu Met Val Asn Gly Ser Met Phe Phe Arg Leu Glu Met Arg
            1060                1065                1070

aat ggt tac cta cat gtg ttc tat gat ttt gga ttc agc agt ggc cgt   3264
Asn Gly Tyr Leu His Val Phe Tyr Asp Phe Gly Phe Ser Ser Gly Arg
        1075                1080                1085

gtg cat ctt gaa gat acg tta aag aaa gct caa att aat gat gca aaa   3312
Val His Leu Glu Asp Thr Leu Lys Lys Ala Gln Ile Asn Asp Ala Lys
   1090                1095                1100

tac cat gag atc tca atc att tac cac aat gat aag aaa atg atc ttg   3360
Tyr His Glu Ile Ser Ile Ile Tyr His Asn Asp Lys Lys Met Ile Leu
1105                1110                1115                1120

gta gtt gac aga agg cat gtc aag agc atg gat aat gaa aag atg aaa   3408
Val Val Asp Arg Arg His Val Lys Ser Met Asp Asn Glu Lys Met Lys
                1125                1130                1135

ata cct ttt aca gat ata tac att gga gga gct cct cca gaa atc tta   3456
Ile Pro Phe Thr Asp Ile Tyr Ile Gly Gly Ala Pro Pro Glu Ile Leu
            1140                1145                1150
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caa tcc agg gcc ctc aga gca cac ctt ccc cta gat atc aac ttc aga   3504
Gln Ser Arg Ala Leu Arg Ala His Leu Pro Leu Asp Ile Asn Phe Arg
       1155                1160                1165

gga tgc atg aag ggc ttc cag ttc caa aag aag gac ttc aat tta ctg   3552
Gly Cys Met Lys Gly Phe Gln Phe Gln Lys Lys Asp Phe Asn Leu Leu
   1170                1175                1180

gag cag aca gaa acc ctg gga gtt ggt tat gga tgc cca gaa gac tca   3600
Glu Gln Thr Glu Thr Leu Gly Val Gly Tyr Gly Cys Pro Glu Asp Ser
1185                1190                1195                1200

ctt ata tct cgc aga gca tat ttc aat gga cag agc ttc att gct tca   3648
Leu Ile Ser Arg Arg Ala Tyr Phe Asn Gly Gln Ser Phe Ile Ala Ser
               1205                1210                1215

att cag aaa ata tct ttc ttt gat ggc ttt gaa gga ggt ttt aat ttc   3696
Ile Gln Lys Ile Ser Phe Phe Asp Gly Phe Glu Gly Gly Phe Asn Phe
          1220                1225                1230

cga aca tta caa cca aat ggg tta cta ttc tat tat gct tca ggg tca   3744
Arg Thr Leu Gln Pro Asn Gly Leu Leu Phe Tyr Tyr Ala Ser Gly Ser
       1235                1240                1245

gac gtg ttc tcc atc tca ctg gat aat ggt act gtc atc atg gat gta   3792
Asp Val Phe Ser Ile Ser Leu Asp Asn Gly Thr Val Ile Met Asp Val
   1250                1255                1260

aag gga atc aaa gtt cag tca gta gat aag cag tac aat gat ggg ctg   3840
Lys Gly Ile Lys Val Gln Ser Val Asp Lys Gln Tyr Asn Asp Gly Leu
1265                1270                1275                1280

tcc cac ttc gtc att agc tct gtc tca ccc aca aga tat gaa ctg ata   3888
Ser His Phe Val Ile Ser Ser Val Ser Pro Thr Arg Tyr Glu Leu Ile
               1285                1290                1295

gta gat aaa agc aga gtt ggg agt aag aat cct acc aaa ggg aaa ata   3936
Val Asp Lys Ser Arg Val Gly Ser Lys Asn Pro Thr Lys Gly Lys Ile
          1300                1305                1310

gaa cag aca caa gca agt gaa aag aag ttt tac ttc ggt ggc tca cca   3984
Glu Gln Thr Gln Ala Ser Glu Lys Lys Phe Tyr Phe Gly Gly Ser Pro
       1315                1320                1325

atc agt gct cag tat gct aat ttc act ggc tgc ata agt aat gcc tac   4032
Ile Ser Ala Gln Tyr Ala Asn Phe Thr Gly Cys Ile Ser Asn Ala Tyr
   1330                1335                1340

ttt acc agg gtg gat aga gat gtg gag gtt gaa gat ttc caa cgg tat   4080
Phe Thr Arg Val Asp Arg Asp Val Glu Val Glu Asp Phe Gln Arg Tyr
1345                1350                1355                1360

act gaa aag gtc cac act tct ctt tat gag tgt ccc att gag tct tca   4128
Thr Glu Lys Val His Thr Ser Leu Tyr Glu Cys Pro Ile Glu Ser Ser
               1365                1370                1375

cca ttg ttt ctc ctc cat aaa aaa gga aaa aat tta tcc aag cct aaa   4176
Pro Leu Phe Leu Leu His Lys Lys Gly Lys Asn Leu Ser Lys Pro Lys
          1380                1385                1390
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gca agt cag aat aaa aag gga ggg aaa agt aaa gat gca cct tca tgg   4224
Ala Ser Gln Asn Lys Lys Gly Gly Lys Ser Lys Asp Ala Pro Ser Trp
       1395                1400                1405

gat cct gtt gct ctg aaa ctc cca gag cgg aat act cca aga aac tct   4272
Asp Pro Val Ala Leu Lys Leu Pro Glu Arg Asn Thr Pro Arg Asn Ser
   1410                1415                1420

cat tgc cac ctt tcc aac agc cct aga gca ata gag cac gcc tat caa   4320
His Cys His Leu Ser Asn Ser Pro Arg Ala Ile Glu His Ala Tyr Gln
1425                1430                1435                1440

tat gga gga aca gcc aac agc cgc caa gag ttt gaa cac tta aaa gga   4368
Tyr Gly Gly Thr Ala Asn Ser Arg Gln Glu Phe Glu His Leu Lys Gly
               1445                1450                1455

gat ttt ggt gcc aaa tct cag ttt tcc att cgt ctg aga act cgt tcc   4416
Asp Phe Gly Ala Lys Ser Gln Phe Ser Ile Arg Leu Arg Thr Arg Ser
           1460                1465                1470

tcc cat ggc atg atc ttc tat gtc tca gat caa gaa gag aat gac ttc   4464
Ser His Gly Met Ile Phe Tyr Val Ser Asp Gln Glu Glu Asn Asp Phe
       1475                1480                1485

atg act cta ttt ttg gcc cat ggc cgc ttg gtt tac atg ttt aat gtt   4512
Met Thr Leu Phe Leu Ala His Gly Arg Leu Val Tyr Met Phe Asn Val
   1490                1495                1500

ggt cac aaa aaa ctg aag att aga agc cag gag aaa tac aat gat ggc   4560
Gly His Lys Lys Leu Lys Ile Arg Ser Gln Glu Lys Tyr Asn Asp Gly
1505                1510                1515                1520

ctg tgg cat gat gtg ata ttt att cga gaa agg agc agt ggc cga ctg   4608
Leu Trp His Asp Val Ile Phe Ile Arg Glu Arg Ser Ser Gly Arg Leu
               1525                1530                1535

gta att gat ggt ctc cga gtc cta gaa gaa agt ctt cct cct act gaa   4656
Val Ile Asp Gly Leu Arg Val Leu Glu Glu Ser Leu Pro Pro Thr Glu
           1540                1545                1550

gct acc tgg aaa atc aag ggt ccc att tat ttg gga ggt gtg gct cct   4704
Ala Thr Trp Lys Ile Lys Gly Pro Ile Tyr Leu Gly Gly Val Ala Pro
       1555                1560                1565

gga aag gct gtg aaa aat gtt cag att aac tcc atc tac agt ttt agt   4752
Gly Lys Ala Val Lys Asn Val Gln Ile Asn Ser Ile Tyr Ser Phe Ser
   1570                1575                1580

ggc tgt ctc agc aat ctc cag ctc aat ggg gcc tcc atc acc tct gct   4800
Gly Cys Leu Ser Asn Leu Gln Leu Asn Gly Ala Ser Ile Thr Ser Ala
1585                1590                1595                1600

tct cag aca ttc agt gtg acc cct tgc ttt gaa ggc ccc atg gaa aca   4848
Ser Gln Thr Phe Ser Val Thr Pro Cys Phe Glu Gly Pro Met Glu Thr
               1605                1610                1615

gga act tac ttt tca aca gaa gga gga tac gtg gtt cta gat gaa tct   4896
Gly Thr Tyr Phe Ser Thr Glu Gly Gly Tyr Val Val Leu Asp Glu Ser
           1620                1625                1630

ttc aat att gga ttg aag ttt gaa att gca ttt gaa gtc cgt ccc aga   4944
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Phe Asn Ile Gly Leu Lys Phe Glu Ile Ala Phe Glu Val Arg Pro Arg
       1635                1640                1645

agc agt tcc gga acc ctg gtc cac ggc cac agt gtc aat ggg gag tac   4992
Ser Ser Ser Gly Thr Leu Val His Gly His Ser Val Asn Gly Glu Tyr
   1650                1655                1660

cta aat gtt cac atg aaa aat gga cag gtc ata gtg aaa gtc aat aat   5040
Leu Asn Val His Met Lys Asn Gly Gln Val Ile Val Lys Val Asn Asn
1665                1670                1675                1680

ggc atc aga gat ttt tcc acc tca gta aca ccc aag cag agt ctc tgt   5088
Gly Ile Arg Asp Phe Ser Thr Ser Val Thr Pro Lys Gln Ser Leu Cys
               1685                1690                1695

gat ggc aga tgg cac aga att aca gtt att aga gat tct aat gtg gtt   5136
Asp Gly Arg Trp His Arg Ile Thr Val Ile Arg Asp Ser Asn Val Val
          1700                1705                1710

cag ttg gat gtg gac tct gaa gtg aac cat gtg gtt gga ccc ctg aat   5184
Gln Leu Asp Val Asp Ser Glu Val Asn His Val Val Gly Pro Leu Asn
       1715                1720                1725

cca aaa cca att gat cac agg gag cct gtg ttt gtt gga ggt gtt cca   5232
Pro Lys Pro Ile Asp His Arg Glu Pro Val Phe Val Gly Gly Val Pro
   1730                1735                1740

gaa tct cta ctg aca cca cgc ttg gcc ccc agc aaa ccc ttc aca ggc   5280
Glu Ser Leu Leu Thr Pro Arg Leu Ala Pro Ser Lys Pro Phe Thr Gly
1745                1750                1755                1760

tgc ata cgc cac ttt gtg att gat gga cac cca gtg agc ttc agt aaa   5328
Cys Ile Arg His Phe Val Ile Asp Gly His Pro Val Ser Phe Ser Lys
               1765                1770                1775

gca gcc ctg gtc agc ggc gcc gta agc atc aac tcc tgt cca gca gcc   5376
Ala Ala Leu Val Ser Gly Ala Val Ser Ile Asn Ser Cys Pro Ala Ala
          1780                1785                1790

tgacatgaca gagcacagct gcccaaatac aaagttcttt agagcactga aagaaacaca 5436

aagccagcca ggaggaacag taactcttcc ttcgggtgga agctttcatc gagttgaaca 5496

ggacttaaac gaatcatcag ggaccggata tttcttattt ctcatttgga ttcttaacct 5556

tgaatccaaa gtgtctgcaa tggacaacaa ttgaaggaga ggcaaactta cttgtattga 5616

gagcacacgc aattcctact ggtgaaatta ctgtttctgt ttctaataaa atagaaggga 5676

ttccaaataa acacttgcac acatttttga agtgcggcta gattctcaga ttcacctttc 5736

ttccagggaa gataactttc aatctatata aaaatctctg tcctaaaact acctttcttt 5796

attttgaaga gacttactaa cttacatata atctaaatta gatgatagat ttctttttag 5856

ccctttttgtt tggtctatca gtataagaag aatattttag gtttatagct gaagttatca 5916

aggtttaata aagtaaattt ctaaca                                      5942
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  1               5                  10                  15

Ala Val Gly Arg Gln Asp Pro Pro Glu Thr Ser Glu Pro Arg Val Ala
             20                  25                  30

Leu Gly Arg Leu Pro Pro Ala Ala Glu Lys Cys Asn Ala Gly Phe Phe
         35                  40                  45

His Thr Leu Ser Gly Glu Cys Val Pro Cys Asp Cys Asn Gly Asn Ser
     50                  55                  60

Asn Glu Cys Leu Asp Gly Ser Gly Tyr Cys Val His Cys Gln Arg Asn
 65                  70                  75                  80

Thr Thr Gly Glu His Cys Glu Lys Cys Leu Asp Gly Tyr Ile Gly Asp
                 85                  90                  95

Ser Ile Arg Gly Ala Pro Gln Phe Cys Gln Pro Cys Pro Cys Pro Leu
            100                 105                 110

Pro His Leu Ala Asn Phe Pro Glu Ser Cys Tyr Arg Lys Asn Gly Ala
        115                 120                 125

Val Arg Cys Ile Cys Asn Glu Asn Tyr Ala Gly Pro Asn Cys Glu Arg
    130                 135                 140

Cys Ala Pro Gly Tyr Tyr Gly Asn Pro Phe Leu Ile Gly Ser Thr Cys
145                 150                 155                 160

Lys Lys Cys Asp Cys Ser Gly Asn Ser Asp Pro Asn Leu Ile Phe Glu
                165                 170                 175

Asp Cys Asp Glu Val Thr Gly Gln Cys Arg Asn Cys Leu Arg Asn Thr
            180                 185                 190

Thr Gly Phe Lys Cys Glu Arg Cys Ala Pro Gly Tyr Tyr Gly Asp Ala
        195                 200                 205

Arg Ile Ala Lys Asn Cys Ala Val Cys Asn Cys Gly Gly Gly Pro Cys
    210                 215                 220

Asp Ser Val Thr Gly Glu Cys Leu Glu Glu Gly Phe Glu Pro Pro Thr
225                 230                 235                 240

Gly Cys Asp Lys Cys Val Trp Asp Leu Thr Asp Asp Leu Arg Leu Ala
                245                 250                 255

Ala Leu Ser Ile Glu Glu Gly Lys Ser Gly Val Leu Ser Val Ser Ser
            260                 265                 270

Gly Ala Ala Ala His Arg His Val Asn Glu Ile Asn Ala Thr Ile Tyr
        275                 280                 285

Leu Leu Lys Thr Lys Leu Ser Glu Arg Glu Asn Gln Tyr Ala Leu Arg
    290                 295                 300
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Lys Ile Gln Ile Asn Asn Ala Glu Asn Thr Met Lys Ser Leu Leu Ser
305                 310                 315                 320

Asp Val Glu Glu Leu Val Glu Lys Glu Asn Gln Ala Ser Arg Lys Gly
                325                 330                 335

Gln Leu Val Gln Lys Glu Ser Met Asp Thr Ile Asn His Ala Ser Gln
            340                 345                 350

Leu Val Glu Gln Ala His Asp Met Arg Asp Lys Ile Gln Glu Ile Asn
        355                 360                 365

Asn Lys Met Leu Tyr Tyr Gly Glu Glu His Glu Leu Ser Pro Lys Glu
    370                 375                 380

Ile Ser Glu Lys Leu Val Leu Ala Gln Lys Met Leu Glu Glu Ile Arg
385                 390                 395                 400

Ser Arg Gln Pro Phe Phe Thr Gln Arg Glu Leu Val Asp Glu Glu Ala
                405                 410                 415

Asp Glu Ala Tyr Glu Leu Leu Ser Gln Ala Glu Ser Trp Gln Arg Leu
            420                 425                 430

His Asn Glu Thr Arg Thr Leu Phe Pro Val Val Leu Glu Gln Leu Asp
        435                 440                 445

Asp Tyr Asn Ala Lys Leu Ser Asp Leu Gln Glu Ala Leu Asp Gln Ala
    450                 455                 460

Leu Asn Tyr Val Arg Asp Ala Glu Asp Met Asn Arg Ala Thr Ala Ala
465                 470                 475                 480

Arg Gln Arg Asp His Glu Lys Gln Gln Glu Arg Val Arg Glu Gln Met
                485                 490                 495

Glu Val Val Asn Met Ser Leu Ser Thr Ser Ala Asp Ser Leu Thr Thr
            500                 505                 510

Pro Arg Leu Thr Leu Ser Glu Leu Asp Asp Ile Ile Lys Asn Ala Ser
        515                 520                 525

Gly Ile Tyr Ala Glu Ile Asp Gly Ala Lys Ser Glu Leu Gln Val Lys
    530                 535                 540

Leu Ser Asn Leu Ser Asn Leu Ser His Asp Leu Val Gln Glu Ala Ile
545                 550                 555                 560

Asp His Ala Gln Asp Leu Gln Gln Glu Ala Asn Glu Leu Ser Arg Lys
                565                 570                 575

Leu His Ser Ser Asp Met Asn Gly Leu Val Gln Lys Ala Leu Asp Ala
            580                 585                 590

Ser Asn Val Tyr Glu Asn Il  Val Asn Tyr Val Ser Glu Ala Asn Glu
        595                 600                 605

Thr Ala Glu Phe Ala Leu Asn Thr Thr Asp Arg Ile Tyr Asp Ala Val
    610                 615                 620
```

Ser Gly Ile Asp Thr Gln Ile Ile Tyr His Lys Asp Glu Ser Glu Asn
625 630 635 640

Leu Leu Asn Gln Ala Arg Glu Leu Gln Ala Lys Ala Glu Ser Ser Ser
645 650 655

Asp Glu Ala Val Ala Asp Thr Ser Arg Arg Val Gly Gly Ala Leu Ala
660 665 670

Arg Lys Ser Ala Leu Lys Thr Arg Leu Ser Asp Ala Val Lys Gln Leu
675 680 685

Gln Ala Ala Glu Arg Gly Asp Ala Gln Gln Arg Leu Gly Gln Ser Arg
690 695 700

Leu Ile Thr Glu Glu Ala Asn Arg Thr Thr Met Glu Val Gln Gln Ala
705 710 715 720

Thr Ala Pro Met Ala Asn Asn Leu Thr Asn Trp Ser Gln Asn Leu Gln
725 730 735

His Phe Asp Ser Ser Ala Tyr Asn Thr Ala Val Asn Ser Ala Arg Asp
740 745 750

Ala Val Arg Asn Leu Thr Glu Val Val Pro Gln Leu Leu Asp Gln Leu
755 760 765

Arg Thr Val Glu Gln Lys Arg Pro Ala Ser Asn Val Ser Ala Ser Ile
770 775 780

Gln Arg Ile Arg Glu Leu Ile Ala Gln Thr Arg Ser Val Ala Ser Lys
785 790 795 800

Ile Gln Val Ser Met Met Phe Asp Gly Gln Ser Ala Val Glu Val His
805 810 815

Ser Arg Thr Ser Met Asp Asp Leu Lys Ala Phe Thr Ser Leu Ser Leu
820 825 830

Tyr Met Lys Pro Pro Val Lys Arg Pro Glu Leu Thr Glu Thr Ala Asp
835 840 845

Gln Phe Ile Leu Tyr Leu Gly Ser Lys Asn Ala Lys Lys Glu Tyr Met
850 855 860

Gly Leu Ala Ile Lys Asn Asp Asn Leu Val Tyr Val Tyr Asn Leu Gly
865 870 875 880

Thr Lys Asp Val Glu Ile Pro Leu Asp Ser Lys Pro Val Ser Ser Trp
885 890 895

Pro Ala Tyr Phe Ser Ile Val Lys Ile Glu Arg Val Gly Lys His Gly
900 905 910

Lys Val Phe Leu Thr Val Pro Ser Leu Ser Ser Thr Ala Glu Glu Lys
915 920 925

Phe Ile Lys Lys Gly Glu Phe Ser Gly Asp Asp Ser Leu Leu Asp Leu
930 935 940

Asp Pro Glu Asp Thr Val Phe Tyr Val Gly Gly Val Pro Ser Asn Phe

945 950 955 960

Lys Leu Pro Thr Ser Leu Asn Leu Pro Gly Phe Val Gly Cys Leu Glu
965 970 975

Leu Ala Thr Leu Asn Asn Asp Val Ile Ser Leu Tyr Asn Phe Lys His
980 985 990

Ile Tyr Asn Met Asp Pro Ser Thr Ser Val Pro Cys Ala Arg Asp Lys
995 1000 1005

Leu Ala Phe Thr Gln Ser Arg Ala Ala Ser Tyr Phe Phe Asp Gly Ser
1010 1015 1020

Gly Tyr Ala Val Val Arg Asp Ile Pro Arg Arg Gly Lys Phe Gly Gln
1025 1030 1035 1040

Val Thr Arg Phe Asp Ile Glu Val Arg Thr Pro Ala Asp Asn Gly Leu
1045 1050 1055

Ile Leu Leu Met Val Asn Gly Ser Met Phe Phe Arg Leu Glu Met Arg
1060 1065 1070

Asn Gly Tyr Leu His Val Phe Tyr Asp Phe Gly Phe Ser Ser Gly Arg
1075 1080 1085

Val His Leu Glu Asp Thr Leu Lys Lys Ala Gln Ile Asn Asp Ala Lys
1090 1095 1100

Tyr His Glu Ile Ser Ile Ile Tyr His Asn Asp Lys Lys Met Ile Leu
1105 1110 1115 1120

Val Val Asp Arg Arg His Val Lys Ser Met Asp Asn Glu Lys Met Lys
1125 1130 1135

Ile Pro Phe Thr Asp Ile Tyr Ile Gly Gly Ala Pro Pro Glu Ile Leu
1140 1145 1150

Gln Ser Arg Ala Leu Arg Ala His Leu Pro Leu Asp Ile Asn Phe Arg
1155 1160 1165

Gly Cys Met Lys Gly Phe Gln Phe Gln Lys Lys Asp Phe Asn Leu Leu
1170 1175 1180

Glu Gln Thr Glu Thr Leu Gly Val Gly Tyr Gly Cys Pro Glu Asp Ser
1185 1190 1195 1200

Leu Ile Ser Arg Arg Ala Tyr Phe Asn Gly Gln Ser Phe Ile Ala Ser
1205 1210 1215

Ile Gln Lys Ile Ser Phe Phe Asp Gly Phe Glu Gly Gly Phe Asn Phe
1220 1225 1230

Arg Thr Leu Gln Pro Asn Gly Leu Leu Phe Tyr Tyr Ala Ser Gly Ser
1235 1240 1245

Asp Val Phe Ser Ile Ser Leu Asp Asn Gly Thr Val Ile Met Asp Val
1250 1255 1260

Lys Gly Ile Lys Val Gln Ser Val Asp Lys Gln Tyr Asn Asp Gly Leu
1265 1270 1275 1280

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Ser His Phe Val Ile Ser Ser Val Ser Pro Thr Arg Tyr Glu Leu Ile
                1285                1290                1295

Val Asp Lys Ser Arg Val Gly Ser Lys Asn Pro Thr Lys Gly Lys Ile
            1300                1305                1310

Glu Gln Thr Gln Ala Ser Glu Lys Lys Phe Tyr Phe Gly Gly Ser Pro
        1315                1320                1325

Ile Ser Ala Gln Tyr Ala Asn Phe Thr Gly Cys Ile Ser Asn Ala Tyr
    1330                1335                1340

Phe Thr Arg Val Asp Arg Asp Val Glu Val Glu Asp Phe Gln Arg Tyr
1345                1350                1355                1360

Thr Glu Lys Val His Thr Ser Leu Tyr Glu Cys Pro Ile Glu Ser Ser
                1365                1370                1375

Pro Leu Phe Leu Leu His Lys Lys Gly Lys Asn Leu Ser Lys Pro Lys
            1380                1385                1390

Ala Ser Gln Asn Lys Lys Gly Gly Lys Ser Lys Asp Ala Pro Ser Trp
        1395                1400                1405

Asp Pro Val Ala Leu Lys Leu Pro Glu Arg Asn Thr Pro Arg Asn Ser
    1410                1415                1420

His Cys His Leu Ser Asn Ser Pro Arg Ala Ile Glu His Ala Tyr Gln
1425                1430                1435                1440

Tyr Gly Gly Thr Ala Asn Ser Arg Gln Glu Phe Glu His Leu Lys Gly
                1445                1450                1455

Asp Phe Gly Ala Lys Ser Gln Phe Ser Ile Arg Leu Arg Thr Arg Ser
            1460                1465                1470

Ser His Gly Met Ile Phe Tyr Val Ser Asp Gln Glu Glu Asn Asp Phe
        1475                1480                1485

Met Thr Leu Phe Leu Ala His Gly Arg Leu Val Tyr Met Phe Asn Val
    1490                1495                1500

Gly His Lys Lys Leu Lys Ile Arg Ser Gln Glu Lys Tyr Asn Asp Gly
1505                1510                1515                1520

Leu Trp His Asp Val Ile Phe Ile Arg Glu Arg Ser Ser Gly Arg Leu
                1525                1530                1535

Val Ile Asp Gly Leu Arg Val Leu Glu Glu Ser Leu Pro Pro Thr Glu
            1540                1545                1550

Ala Thr Trp Lys Ile Lys Gly Pro Ile Tyr Leu Gly Gly Val Ala Pro
        1555                1560                1565

Gly Lys Ala Val Lys Asn Val Gln Ile Asn Ser Ile Tyr Ser Phe Ser
    1570                1575                1580

Gly Cys Leu Ser Asn Leu Gln Leu Asn Gly Ala Ser Ile Thr Ser Ala
1585                1590                1595                1600
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Ser Gln Thr Phe Ser Val Thr Pro Cys Phe Glu Gly Pro Met Glu Thr
                1605                1610                1615

Gly Thr Tyr Phe Ser Thr Glu Gly Gly Tyr Val Val Leu Asp Glu Ser
            1620                1625                1630

Phe Asn Ile Gly Leu Lys Phe Glu Ile Ala Phe Glu Val Arg Pro Arg
        1635                1640                1645

Ser Ser Ser Gly Thr Leu Val His Gly His Ser Val Asn Gly Glu Tyr
    1650                1655                1660

Leu Asn Val His Met Lys Asn Gly Gln Val Ile Val Lys Val Asn Asn
1665                1670                1675                1680

Gly Ile Arg Asp Phe Ser Thr Ser Val Thr Pro Lys Gln Ser Leu Cys
                1685                1690                1695

Asp Gly Arg Trp His Arg Ile Thr Val Ile Arg Asp Ser Asn Val Val
            1700                1705                1710

Gln Leu Asp Val Asp Ser Glu Val Asn His Val Val Gly Pro Leu Asn
        1715                1720                1725

Pro Lys Pro Ile Asp His Arg Glu Pro Val Phe Val Gly Gly Val Pro
    1730                1735                1740

Glu Ser Leu Leu Thr Pro Arg Leu Ala Pro Ser Lys Pro Phe Thr Gly
1745                1750                1755                1760

Cys Ile Arg His Phe Val Ile Asp Gly His Pro Val Ser Phe Ser Lys
                1765                1770                1775

Ala Ala Leu Val Ser Gly Ala Val Ser Ile Asn Ser Cys Pro Ala Ala
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                  Met Ala Leu Ser Ser Ala Trp Arg Ser Val Leu Pro
                    1               5                  10

ctg tgg ctc ctc tgg agc gct gcc tgc tcc cgc gcc gcg tcc ggg gac   100
Leu Trp Leu Leu Trp Ser Ala Ala Cys Ser Arg Ala Ala Ser Gly Asp
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        15                  20                  25

gac aac gct ttt cct ttt gac att gaa ggg agc tca gcg gtt ggc agg   148
Asp Asn Ala Phe Pro Phe Asp Ile Glu Gly Ser Ser Ala Val Gly Arg
     30                  35                  40

caa gac ccg cct gag acg agc gaa ccc cgc gtg gct ctg gga cgc ctg   196
Gln Asp Pro Pro Glu Thr Ser Glu Pro Arg Val Ala Leu Gly Arg Leu
 45                  50                  55                  60

ccg cct gcg gcc gag aaa tgc aat gct gga ttc ttt cac acc ctg tcg   244
Pro Pro Ala Ala Glu Lys Cys Asn Ala Gly Phe Phe His Thr Leu Ser
                 65                  70                  75

gga gaa tgt gtg ccc tgc gac tgt aat ggc aat tcc aac gag tgt ttg   292
Gly Glu Cys Val Pro Cys Asp Cys Asn Gly Asn Ser Asn Glu Cys Leu
             80                  85                  90

gac ggc tca gga tac tgt gtg cac tgc cag cgg aac aca aca gga gag   340
Asp Gly Ser Gly Tyr Cys Val His Cys Gln Arg Asn Thr Thr Gly Glu
         95                  100                 105

cac tgt gaa aag tgt ctg gat ggt tat atc gga gat tcc atc agg gga   388
His Cys Glu Lys Cys Leu Asp Gly Tyr Ile Gly Asp Ser Ile Arg Gly
    110                 115                 120

gca ccc caa ttc tgc cag ccg tgc ccc tgt ccc ctg ccc cac ttg gcc   436
Ala Pro Gln Phe Cys Gln Pro Cys Pro Cys Pro Leu Pro His Leu Ala
125                 130                 135                 140

aat ttt cca gaa tcc tgc tat agg aaa aat gga gct gtt cgg tgc att   484
Asn Phe Pro Glu Ser Cys Tyr Arg Lys Asn Gly Ala Val Arg Cys Ile
                145                 150                 155

tgt aac gaa aat tat gct gga cct aac tgt gaa aga tgt gct ccc ggt   532
Cys Asn Glu Asn Tyr Ala Gly Pro Asn Cys Glu Arg Cys Ala Pro Gly
            160                 165                 170

tac tat gga aac ccc ttc ctc att gga agc acc tgt aag aaa tgt gac   580
Tyr Tyr Gly Asn Pro Phe Leu Ile Gly Ser Thr Cys Lys Lys Cys Asp
        175                 180                 185

tgc agt gga aat tca gat ccc aac ctg atc ttt gaa gat tgt gat gaa   628
Cys Ser Gly Asn Ser Asp Pro Asn Leu Ile Phe Glu Asp Cys Asp Glu
    190                 195                 200

gtc act ggc cag tgt agg aat tgc tta cgc aac acc acc gga ttc aag   676
Val Thr Gly Gln Cys Arg Asn Cys Leu Arg Asn Thr Thr Gly Phe Lys
205                 210                 215                 220

tgt gaa cgt tgc gct cct ggc tac tat ggg gac gcc agg ata gcc aag   724
Cys Glu Arg Cys Ala Pro Gly Tyr Tyr Gly Asp Ala Arg Ile Ala Lys
                225                 230                 235

aac tgt gca gtg tgc aac tgc ggg gga ggc cca tgt gac agt gta acc   772
Asn Cys Ala Val Cys Asn Cys Gly Gly Gly Pro Cys Asp Ser Val Thr
            240                 245                 250

gga gaa tgc ttg gaa gaa ggt ttt gaa ccc cct aca ggc tgt gat aag   820
Gly Glu Cys Leu Glu Glu Gly Phe Glu Pro Pro Thr Gly Cys Asp Lys
        255                 260                 265
```

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tgc gtc tgg gac ctg act gat gac ctg cgg tta gca gcg ctc tcc atc   868
Cys Val Trp Asp Leu Thr Asp Asp Leu Arg Leu Ala Ala Leu Ser Ile
    270                 275                 280

gag gaa ggc aaa tcc ggg gtg ctg agc gta tcc tct ggg gcc gcc gct   916
Glu Glu Gly Lys Ser Gly Val Leu Ser Val Ser Ser Gly Ala Ala Ala
285                 290                 295                 300

cat agg cac gtg aat gaa atc aac gcc acc atc tac ctc ctc aaa aca   964
His Arg His Val Asn Glu Ile Asn Ala Thr Ile Tyr Leu Leu Lys Thr
                305                 310                 315

aaa ttg tca gaa aga gaa aac caa tac gcc cta aga aag ata caa atc   1012
Lys Leu Ser Glu Arg Glu Asn Gln Tyr Ala Leu Arg Lys Ile Gln Ile
            320                 325                 330

aac aat gct gag aac acg atg aaa agc ctt ctg tct gac gta gag gaa   1060
Asn Asn Ala Glu Asn Thr Met Lys Ser Leu Leu Ser Asp Val Glu Glu
        335                 340                 345

tta gtt gaa aag gaa aat caa gcc tcc aga aaa gga caa ctt gtt cag   1108
Leu Val Glu Lys Glu Asn Gln Ala Ser Arg Lys Gly Gln Leu Val Gln
    350                 355                 360

aag gaa agc atg gac acc att aac cac gca agt cag ctg gta gag caa   1156
Lys Glu Ser Met Asp Thr Ile Asn His Ala Ser Gln Leu Val Glu Gln
365                 370                 375                 380

gcc cat gat atg agg gat aaa atc caa gag atc aac aac aag atg ctc   1204
Ala His Asp Met Arg Asp Lys Ile Gln Glu Ile Asn Asn Lys Met Leu
                385                 390                 395

tat tat ggg gaa gag cat gaa ctt agc ccc aag gaa atc tct gag aag   1252
Tyr Tyr Gly Glu Glu His Glu Leu Ser Pro Lys Glu Ile Ser Glu Lys
            400                 405                 410

ctg gtg ttg gcc cag aag atg ctt gaa gag att aga agc cgt caa cca   1300
Leu Val Leu Ala Gln Lys Met Leu Glu Glu Ile Arg Ser Arg Gln Pro
        415                 420                 425

ttt ttc acc caa cgg gag ctc gtg gat gag gag gca gat gag gct tac   1348
Phe Phe Thr Gln Arg Glu Leu Val Asp Glu Glu Ala Asp Glu Ala Tyr
    430                 435                 440

gaa cta ctg agc cag gct gag agc tgg cag cgg ctg cac aat gag acc   1396
Glu Leu Leu Ser Gln Ala Glu Ser Trp Gln Arg Leu His Asn Glu Thr
445                 450                 455                 460

cgc act ctg ttt cct gtc gtc ctg gag cag ctg gat gac tac aat gct   1444
Arg Thr Leu Phe Pro Val Val Leu Glu Gln Leu Asp Asp Tyr Asn Ala
                465                 470                 475

aag ttg tca gat ctc cag gaa gca ctt gac cag gcc ctt aac tat gtc   1492
Lys Leu Ser Asp Leu Gln Glu Ala Leu Asp Gln Ala Leu Asn Tyr Val
            480                 485                 490

agg gat gcc gaa gac atg aac agg gcc aca gca gcc agg cag cgg gac   1540
Arg Asp Ala Glu Asp Met Asn Arg Ala Thr Ala Ala Arg Gln Arg Asp
        495                 500                 505
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cat gag aaa caa cag gaa aga gtg agg gaa caa atg gaa gtg gtg aac   1588
His Glu Lys Gln Gln Glu Arg Val Arg Glu Gln Met Glu Val Val Asn
    510                 515                 520

atg tct ctg agc aca tct gcg gac tct ctg aca aca cct cgt cta act   1636
Met Ser Leu Ser Thr Ser Ala Asp Ser Leu Thr Thr Pro Arg Leu Thr
525                 530                 535                 540

ctt tca gaa ctt gat gat ata ata aag aat gcg tca ggg att tat gca   1684
Leu Ser Glu Leu Asp Asp Ile Ile Lys Asn Ala Ser Gly Ile Tyr Ala
                545                 550                 555

gaa ata gat gga gcc aaa agt gaa cta caa gta aaa cta tct aac cta   1732
Glu Ile Asp Gly Ala Lys Ser Glu Leu Gln Val Lys Leu Ser Asn Leu
            560                 565                 570

agt aac ctc agc cat gat tta gtc caa gaa gct att gac cat gca cag   1780
Ser Asn Leu Ser His Asp Leu Val Gln Glu Ala Ile Asp His Ala Gln
        575                 580                 585

gac ctt caa caa gaa gct aat gaa ttg agc agg aag ttg cac agt tca   1828
Asp Leu Gln Gln Glu Ala Asn Glu Leu Ser Arg Lys Leu His Ser Ser
    590                 595                 600

gat atg aac ggg ctg gta cag aag gct ttg gat gca tca aat gtc tat   1876
Asp Met Asn Gly Leu Val Gln Lys Ala Leu Asp Ala Ser Asn Val Tyr
605                 610                 615                 620

gaa aat att gtt aat tat gtt agt gaa gcc aat gaa aca gca gaa ttt   1924
Glu Asn Ile Val Asn Tyr Val Ser Glu Ala Asn Glu Thr Ala Glu Phe
                625                 630                 635

gct ttg aac acc act gac cga att tat gat gcg gtg agt ggg att gat   1972
Ala Leu Asn Thr Thr Asp Arg Ile Tyr Asp Ala Val Ser Gly Ile Asp
            640                 645                 650

act caa atc att tac cat aaa gat gaa agt gag aac ctc ctc aat caa   2020
Thr Gln Ile Ile Tyr His Lys Asp Glu Ser Glu Asn Leu Leu Asn Gln
        655                 660                 665

gcc aga gaa ctg caa gca aag gca gag tct agc agt gat gaa gca gtg   2068
Ala Arg Glu Leu Gln Ala Lys Ala Glu Ser Ser Ser Asp Glu Ala Val
    670                 675                 680

gct gac act agc agg cgt gtg ggt gga gcc cta gca agg aaa agt gcc   2116
Ala Asp Thr Ser Arg Arg Val Gly Gly Ala Leu Ala Arg Lys Ser Ala
685                 690                 695                 700

ctt aaa acc aga ctc agt gat gcc gtt aag caa cta caa gca gca gag   2164
Leu Lys Thr Arg Leu Ser Asp Ala Val Lys Gln Leu Gln Ala Ala Glu
                705                 710                 715

aga ggg gat gcc cag cag cgc ctg ggg cag tct aga ctg atc acc gag   2212
Arg Gly Asp Ala Gln Gln Arg Leu Gly Gln Ser Arg Leu Ile Thr Glu
            720                 725                 730

gaa gcc aac agg acg acg atg gag gtg cag cag gcc act gcc ccc atg   2260
Glu Ala Asn Arg Thr Thr Met Glu Val Gln Gln Ala Thr Ala Pro Met
        735                 740                 745

gcc aac aat cta acc aac tgg tca cag aat ctt caa cat ttt gac tct   2308
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```
Ala Asn Asn Leu Thr Asn Trp Ser Gln Asn Leu Gln His Phe Asp Ser
    750                 755                 760

tct gct tac aac act gca gtg aac tct gct agg gat gca gta aga aat   2356
Ser Ala Tyr Asn Thr Ala Val Asn Ser Ala Arg Asp Ala Val Arg Asn
765                 770                 775                 780

ctg acc gag gtt gtc cct cag ctc ctg gat cag ctt cgt acg gtt gag   2404
Leu Thr Glu Val Val Pro Gln Leu Leu Asp Gln Leu Arg Thr Val Glu
                785                 790                 795

cag aag cga cct gca agc aac gtt tct gcc agc atc cag agg atc cga   2452
Gln Lys Arg Pro Ala Ser Asn Val Ser Ala Ser Ile Gln Arg Ile Arg
            800                 805                 810

gag ctc att gct cag acc aga agt gtt gcc agc aag atc caa gtc tcc   2500
Glu Leu Ile Ala Gln Thr Arg Ser Val Ala Ser Lys Ile Gln Val Ser
        815                 820                 825

atg atg ttt gat ggc cag tca gct gtg gaa gtg cac tcg aga acc agt   2548
Met Met Phe Asp Gly Gln Ser Ala Val Glu Val His Ser Arg Thr Ser
    830                 835                 840

atg gat gac tta aag gcc ttc acg tct ctg agc ctg tac atg aaa ccc   2596
Met Asp Asp Leu Lys Ala Phe Thr Ser Leu Ser Leu Tyr Met Lys Pro
845                 850                 855                 860

cct gtg aag cgg ccg gaa ctg acc gag act gca gat cag ttt atc ctg   2644
Pro Val Lys Arg Pro Glu Leu Thr Glu Thr Ala Asp Gln Phe Ile Leu
                865                 870                 875

tac ctc gga agc aaa aac gcc aaa aaa gag tat atg ggt ctt gca atc   2692
Tyr Leu Gly Ser Lys Asn Ala Lys Lys Glu Tyr Met Gly Leu Ala Ile
            880                 885                 890

aaa aat gat aat ctg gta tac gtc tat aat ttg gga act aaa gat gtg   2740
Lys Asn Asp Asn Leu Val Tyr Val Tyr Asn Leu Gly Thr Lys Asp Val
        895                 900                 905

gag att ccc ctg gac tcc aag ccc gtc agt tcc tgg cct gct tac ttc   2788
Glu Ile Pro Leu Asp Ser Lys Pro Val Ser Ser Trp Pro Ala Tyr Phe
    910                 915                 920

agc att gtc aag att gaa agg gtg gga aaa cat gga aag gtg ttt tta   2836
Ser Ile Val Lys Ile Glu Arg Val Gly Lys His Gly Lys Val Phe Leu
925                 930                 935                 940

aca gtc ccg agt cta agt agc aca gca gag gaa aag ttc att aaa aag   2884
Thr Val Pro Ser Leu Ser Ser Thr Ala Glu Glu Lys Phe Ile Lys Lys
                945                 950                 955

ggg gaa ttt tcg gga gat gac tct ctg ctg gac ctg gac cct gag gac   2932
Gly Glu Phe Ser Gly Asp Asp Ser Leu Leu Asp Leu Asp Pro Glu Asp
            960                 965                 970

aca gtg ttt tat gtt ggt gga gtg cct tcc aac ttc aag ctc cct acc   2980
Thr Val Phe Tyr Val Gly Gly Val Pro Ser Asn Phe Lys Leu Pro Thr
        975                 980                 985

agc tta aac ctg cct ggc ttt gtt ggc tgc ctg gaa ctg gcc act ttg   3028
Ser Leu Asn Leu Pro Gly Phe Val Gly Cys Leu Glu Leu Ala Thr Leu
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    990                 995                1000

aat aat gat gtg atc agc ttg tac aac ttt aag cac atc tat aat atg   3076
Asn Asn Asp Val Ile Ser Leu Tyr Asn Phe Lys His Ile Tyr Asn Met
1005              1010                1015                1020

gac ccc tcc aca tca gtg cca tgt gcc cga gat aag ctg gcc ttc act   3124
Asp Pro Ser Thr Ser Val Pro Cys Ala Arg Asp Lys Leu Ala Phe Thr
                1025                1030                1035

cag agt cgg gct gcc agt tac ttc ttc gat ggc tcc ggt tat gcc gtg   3172
Gln Ser Arg Ala Ala Ser Tyr Phe Phe Asp Gly Ser Gly Tyr Ala Val
           1040                1045                1050

gtg aga gac ata cca agg aga ggg aaa ttt ggt cag gtg act cgc ttt   3220
Val Arg Asp Ile Pro Arg Arg Gly Lys Phe Gly Gln Val Thr Arg Phe
       1055                1060                1065

gac ata gaa gtt cga aca cca gct gac aac ggc ctt att ctc ctg atg   3268
Asp Ile Glu Val Arg Thr Pro Ala Asp Asn Gly Leu Ile Leu Leu Met
   1070                1075                1080

gtc aat gga agt atg ttt ttc aga ctg gaa atg cgc aat ggt tac cta   3316
Val Asn Gly Ser Met Phe Phe Arg Leu Glu Met Arg Asn Gly Tyr Leu
1085              1090                1095                1100

cat gtg ttc tat gat ttt gga ttc agc agt ggc cgt gtg cat ctt gaa   3364
His Val Phe Tyr Asp Phe Gly Phe Ser Ser Gly Arg Val His Leu Glu
                1105                1110                1115

gat acg tta aag aaa gct caa att aat gat gca aaa tac cat gag atc   3412
Asp Thr Leu Lys Lys Ala Gln Ile Asn Asp Ala Lys Tyr His Glu Ile
           1120                1125                1130

tca atc att tac cac aat gat aag aaa atg atc ttg gta gtt gac aga   3460
Ser Ile Ile Tyr His Asn Asp Lys Lys Met Ile Leu Val Val Asp Arg
       1135                1140                1145

agg cat gtc aag agc atg gat aat gaa aag atg aaa ata cct ttt aca   3508
Arg His Val Lys Ser Met Asp Asn Glu Lys Met Lys Ile Pro Phe Thr
   1150                1155                1160

gat ata tac att gga gga gct cct cca gaa atc tta caa tcc agg gcc   3556
Asp Ile Tyr Ile Gly Gly Ala Pro Pro Glu Ile Leu Gln Ser Arg Ala
1165              1170                1175                1180

ctc aga gca cac ctt ccc cta gat atc aac ttc aga gga tgc atg aag   3604
Leu Arg Ala His Leu Pro Leu Asp Ile Asn Phe Arg Gly Cys Met Lys
                1185                1190                1195

ggc ttc cag ttc caa aag aag gac ttc aat tta ctg gag cag aca gaa   3652
Gly Phe Gln Phe Gln Lys Lys Asp Phe Asn Leu Leu Glu Gln Thr Glu
           1200                1205                1210

acc ctg gga gtt ggt tat gga tgc cca gaa gac tca ctt ata tct cgc   3700
Thr Leu Gly Val Gly Tyr Gly Cys Pro Glu Asp Ser Leu Ile Ser Arg
       1215                1220                1225

aga gca tat ttc aat gga cag agc ttc att gct tca att cag aaa ata   3748
Arg Ala Tyr Phe Asn Gly Gln Ser Phe Ile Ala Ser Ile Gln Lys Ile
   1230                1235                1240
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tct ttc ttt gat ggc ttt gaa gga ggt ttt aat ttc cga aca tta caa   3796
Ser Phe Phe Asp Gly Phe Glu Gly Gly Phe Asn Phe Arg Thr Leu Gln
1245              1250                1255                1260

cca aat ggg tta cta ttc tat tat gct tca ggg tca gac gtg ttc tcc   3844
Pro Asn Gly Leu Leu Phe Tyr Tyr Ala Ser Gly Ser Asp Val Phe Ser
                1265                1270                1275

atc tca ctg gat aat ggt act gtc atc atg gat gta aag gga atc aaa   3892
Ile Ser Leu Asp Asn Gly Thr Val Ile Met Asp Val Lys Gly Ile Lys
          1280                1285                1290

gtt cag tca gta gat aag cag tac aat gat ggg ctg tcc cac ttc gtc   3940
Val Gln Ser Val Asp Lys Gln Tyr Asn Asp Gly Leu Ser His Phe Val
       1295                1300                1305

att agc tct gtc tca ccc aca aga tat gaa ctg ata gta gat aaa agc   3988
Ile Ser Ser Val Ser Pro Thr Arg Tyr Glu Leu Ile Val Asp Lys Ser
   1310                1315                1320

aga gtt ggg agt aag aat cct acc aaa ggg aaa ata gaa cag aca caa   4036
Arg Val Gly Ser Lys Asn Pro Thr Lys Gly Lys Ile Glu Gln Thr Gln
1325                1330                1335                1340

gca agt gaa aag aag ttt tac ttc ggt ggc tca cca atc agt gct cag   4084
Ala Ser Glu Lys Lys Phe Tyr Phe Gly Gly Ser Pro Ile Ser Ala Gln
                1345                1350                1355

tat gct aat ttc act ggc tgc ata agt aat gcc tac ttt acc agg gtg   4132
Tyr Ala Asn Phe Thr Gly Cys Ile Ser Asn Ala Tyr Phe Thr Arg Val
          1360                1365                1370

gat aga gat gtg gag gtt gaa gat ttc caa cgg tat act gaa aag gtc   4180
Asp Arg Asp Val Glu Val Glu Asp Phe Gln Arg Tyr Thr Glu Lys Val
       1375                1380                1385

cac act tct ctt tat gag tgt ccc att gag tct tca cca ttg ttt ctc   4228
His Thr Ser Leu Tyr Glu Cys Pro Ile Glu Ser Ser Pro Leu Phe Leu
   1390                1395                1400

ctc cat aaa aaa gga aaa aat tta tcc aag cct aaa gca agt cag aat   4276
Leu His Lys Lys Gly Lys Asn Leu Ser Lys Pro Lys Ala Ser Gln Asn
1405                1410                1415                1420

aaa aag gga ggg aaa agt aaa gat gca cct tca tgg gat cct gtt gct   4324
Lys Lys Gly Gly Lys Ser Lys Asp Ala Pro Ser Trp Asp Pro Val Ala
                1425                1430                1435

ctg aaa ctc cca gag cgg aat act cca aga aac tct cat tgc cac ctt   4372
Leu Lys Leu Pro Glu Arg Asn Thr Pro Arg Asn Ser His Cys His Leu
          1440                1445                1450

tcc aac agc cct aga gca ata gag cac gcc tat caa tat gga gga aca   4420
Ser Asn Ser Pro Arg Ala Ile Glu His Ala Tyr Gln Tyr Gly Gly Thr
       1455                1460                1465

gcc aac agc cgc caa gag ttt gaa cac tta aaa gga gat ttt ggt gcc   4468
Ala Asn Ser Arg Gln Glu Phe Glu His Leu Lys Gly Asp Phe Gly Ala
   1470                1475                1480
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aaa tct cag ttt tcc att cgt ctg aga act cgt tcc tcc cat ggc atg   4516
Lys Ser Gln Phe Ser Ile Arg Leu Arg Thr Arg Ser Ser His Gly Met
1485                1490                1495                1500

atc ttc tat gtc tca gat caa gaa gag aat gac ttc atg act cta ttt   4564
Ile Phe Tyr Val Ser Asp Gln Glu Glu Asn Asp Phe Met Thr Leu Phe
                1505                1510                1515

ttg gcc cat ggc cgc ttg gtt tac atg ttt aat gtt ggt cac aaa aaa   4612
Leu Ala His Gly Arg Leu Val Tyr Met Phe Asn Val Gly His Lys Lys
            1520                1525                1530

ctg aag att aga agc cag gag aaa tac aat gat ggc ctg tgg cat gat   4660
Leu Lys Ile Arg Ser Gln Glu Lys Tyr Asn Asp Gly Leu Trp His Asp
        1535                1540                1545

gtg ata ttt att cga gaa agg agc agt ggc cga ctg gta att gat ggt   4708
Val Ile Phe Ile Arg Glu Arg Ser Ser Gly Arg Leu Val Ile Asp Gly
    1550                1555                1560

ctc cga gtc cta gaa gaa agt ctt cct cct act gaa gct acc tgg aaa   4756
Leu Arg Val Leu Glu Glu Ser Leu Pro Pro Thr Glu Ala Thr Trp Lys
1565                1570                1575                1580

atc aag ggt ccc att tat ttg gga ggt gtg gct cct gga aag gct gtg   4804
Ile Lys Gly Pro Ile Tyr Leu Gly Gly Val Ala Pro Gly Lys Ala Val
                1585                1590                1595

aaa aat gtt cag att aac tcc atc tac agt ttt agt ggc tgt ctc agc   4852
Lys Asn Val Gln Ile Asn Ser Ile Tyr Ser Phe Ser Gly Cys Leu Ser
            1600                1605                1610

aat ctc cag ctc aat ggg gcc tcc atc acc tct gct tct cag aca ttc   4900
Asn Leu Gln Leu Asn Gly Ala Ser Ile Thr Ser Ala Ser Gln Thr Phe
        1615                1620                1625

agt gtg acc cct tgc ttt gaa ggc ccc atg gaa aca gga act tac ttt   4948
Ser Val Thr Pro Cys Phe Glu Gly Pro Met Glu Thr Gly Thr Tyr Phe
    1630                1635                1640

tca aca gaa gga gga tac gtg gtt cta gat gaa tct ttc aat att gga   4996
Ser Thr Glu Gly Gly Tyr Val Val Leu Asp Glu Ser Phe Asn Ile Gly
1645                1650                1655                1660

ttg aag ttt gaa att gca ttt gaa gtc cgt ccc aga agc agt tcc gga   5044
Leu Lys Phe Glu Ile Ala Phe Glu Val Arg Pro Arg Ser Ser Ser Gly
                1665                1670                1675

acc ctg gtc cac ggc cac agt gtc aat ggg gag tac cta aat gtt cac   5092
Thr Leu Val His Gly His Ser Val Asn Gly Glu Tyr Leu Asn Val His
            1680                1685                1690

atg aaa aat gga cag gtc ata gtg aaa gtc aat aat ggc atc aga gat   5140
Met Lys Asn Gly Gln Val Ile Val Lys Val Asn Asn Gly Ile Arg Asp
        1695                1700                1705

ttt tcc acc tca gta aca ccc aag cag agt ctc tgt gat ggc aga tgg   5188
Phe Ser Thr Ser Val Thr Pro Lys Gln Ser Leu Cys Asp Gly Arg Trp
    1710                1715                1720

cac aga att aca gtt att aga gat tct aat gtg gtt cag ttg gat gtg   5236
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His Arg Ile Thr Val Ile Arg Asp Ser Asn Val Val Gln Leu Asp Val
1725                1730                1735                1740

gac tct gaa gtg aac cat gtg gtt gga ccc ctg aat cca aaa cca att   5284
Asp Ser Glu Val Asn His Val Val Gly Pro Leu Asn Pro Lys Pro Ile
                1745                1750                1755

gat cac agg gag cct gtg ttt gtt gga ggt gtt cca gaa tct cta ctg   5332
Asp His Arg Glu Pro Val Phe Val Gly Gly Val Pro Glu Ser Leu Leu
            1760                1765                1770

aca cca cgc ttg gcc ccc agc aaa ccc ttc aca ggc tgc ata cgc cac   5380
Thr Pro Arg Leu Ala Pro Ser Lys Pro Phe Thr Gly Cys Ile Arg His
        1775                1780                1785

ttt gtg att gat gga cac cca gtg agc ttc agt aaa gca gcc ctg gtc   5428
Phe Val Ile Asp Gly His Pro Val Ser Phe Ser Lys Ala Ala Leu Val
    1790                1795                1800

agc ggc gcc gta agc atc aac tcc tgt cca gca gcc gac tac aag gac   5476
Ser Gly Ala Val Ser Ile Asn Ser Cys Pro Ala Ala Asp Tyr Lys Asp
1805                1810                1815                1820

gac gat gac aag taagcttggc                                       5498
Asp Asp Asp Lys
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Met Ala Leu Ser Ser Ala Trp Arg Ser Val Leu Pro Leu Trp Leu Leu
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Trp Ser Ala Ala Cys Ser Arg Ala Ala Ser Gly Asp Asp Asn Ala Phe
            20                  25                  30

Pro Phe Asp Ile Glu Gly Ser Ser Ala Val Gly Arg Gln Asp Pro Pro
        35                  40                  45

Glu Thr Ser Glu Pro Arg Val Ala Leu Gly Arg Leu Pro Pro Ala Ala
    50                  55                  60

Glu Lys Cys Asn Ala Gly Phe Phe His Thr Leu Ser Gly Glu Cys Val
65                  70                  75                  80

Pro Cys Asp Cys Asn Gly Asn Ser Asn Glu Cys Leu Asp Gly Ser Gly
                85                  90                  95

Tyr Cys Val His Cys Gln Arg Asn Thr Thr Gly Glu His Cys Glu Lys
            100                 105                 110

Cys Leu Asp Gly Tyr Ile Gly Asp Ser Ile Arg Gly Ala Pro Gln Phe
        115                 120                 125

Cys Gln Pro Cys Pro Cys Pro Leu Pro His Leu Ala Asn Phe Pro Glu
    130                 135                 140

Ser Cys Tyr Arg Lys Asn Gly Ala Val Arg Cys Ile Cys Asn Glu Asn
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145                 150                 155                 160

Tyr Ala Gly Pro Asn Cys Glu Arg Cys Ala Pro Gly Tyr Tyr Gly Asn
                165                 170                 175

Pro Phe Leu Ile Gly Ser Thr Cys Lys Lys Cys Asp Cys Ser Gly Asn
            180                 185                 190

Ser Asp Pro Asn Leu Ile Phe Glu Asp Cys Asp Glu Val Thr Gly Gln
        195                 200                 205

Cys Arg Asn Cys Leu Arg Asn Thr Thr Gly Phe Lys Cys Glu Arg Cys
    210                 215                 220

Ala Pro Gly Tyr Tyr Gly Asp Ala Arg Ile Ala Lys Asn Cys Ala Val
225                 230                 235                 240

Cys Asn Cys Gly Gly Gly Pro Cys Asp Ser Val Thr Gly Glu Cys Leu
                245                 250                 255

Glu Glu Gly Phe Glu Pro Pro Thr Gly Cys Asp Lys Cys Val Trp Asp
            260                 265                 270

Leu Thr Asp Asp Leu Arg Leu Ala Ala Leu Ser Ile Glu Glu Gly Lys
        275                 280                 285

Ser Gly Val Leu Ser Val Ser Ser Gly Ala Ala Ala His Arg His Val
    290                 295                 300

Asn Glu Ile Asn Ala Thr Ile Tyr Leu Leu Lys Thr Lys Leu Ser Glu
305                 310                 315                 320

Arg Glu Asn Gln Tyr Ala Leu Arg Lys Ile Gln Ile Asn Asn Ala Glu
                325                 330                 335

Asn Thr Met Lys Ser Leu Leu Ser Asp Val Glu Glu Leu Val Glu Lys
            340                 345                 350

Glu Asn Gln Ala Ser Arg Lys Gly Gln Leu Val Gln Lys Glu Ser Met
        355                 360                 365

Asp Thr Ile Asn His Ala Ser Gln Leu Val Glu Gln Ala His Asp Met
    370                 375                 380

Arg Asp Lys Ile Gln Glu Ile Asn Asn Lys Met Leu Tyr Tyr Gly Glu
385                 390                 395                 400

Glu His Glu Leu Ser Pro Lys Glu Ile Ser Glu Lys Leu Val Leu Ala
                405                 410                 415

Gln Lys Met Leu Glu Glu Ile Arg Ser Arg Gln Pro Phe Phe Thr Gln
            420                 425                 430

Arg Glu Leu Val Asp Glu Glu Ala Asp Glu Ala Tyr Glu Leu Leu Ser
        435                 440                 445

Gln Ala Glu Ser Trp Gln Arg Leu His Asn Glu Thr Arg Thr Leu Phe
    450                 455                 460

Pro Val Val Leu Glu Gln Leu Asp Asp Tyr Asn Ala Lys Leu Ser Asp
465                 470                 475                 480
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Leu Gln Glu Ala Leu Asp Gln Ala Leu Asn Tyr Val Arg Asp Ala Glu
485 490 495

Asp Met Asn Arg Ala Thr Ala Ala Arg Gln Arg Asp His Glu Lys Gln
500 505 510

Gln Glu Arg Val Arg Glu Gln Met Glu Val Val Asn Met Ser Leu Ser
515 520 525

Thr Ser Ala Asp Ser Leu Thr Thr Pro Arg Leu Thr Leu Ser Glu Leu
530 535 540

Asp Asp Ile Ile Lys Asn Ala Ser Gly Ile Tyr Ala Glu Ile Asp Gly
545 550 555 560

Ala Lys Ser Glu Leu Gln Val Lys Leu Ser Asn Leu Ser Asn Leu Ser
565 570 575

His Asp Leu Val Gln Glu Ala Ile Asp His Ala Gln Asp Leu Gln Gln
580 585 590

Glu Ala Asn Glu Leu Ser Arg Lys Leu His Ser Ser Asp Met Asn Gly
595 600 605

Leu Val Gln Lys Ala Leu Asp Ala Ser Asn Val Tyr Glu Asn Ile Val
610 615 620

Asn Tyr Val Ser Glu Ala Asn Glu Thr Ala Glu Phe Ala Leu Asn Thr
625 630 635 640

Thr Asp Arg Ile Tyr Asp Ala Val Ser Gly Ile Asp Thr Gln Ile Ile
645 650 655

Tyr His Lys Asp Glu Ser Glu Asn Leu Leu Asn Gln Ala Arg Glu Leu
660 665 670

Gln Ala Lys Ala Glu Ser Ser Ser Asp Glu Ala Val Ala Asp Thr Ser
675 680 685

Arg Arg Val Gly Gly Ala Leu Ala Arg Lys Ser Ala Leu Lys Thr Arg
690 695 700

Leu Ser Asp Ala Val Lys Gln Leu Gln Ala Ala Glu Arg Gly Asp Ala
705 710 715 720

Gln Gln Arg Leu Gly Gln Ser Arg Leu Ile Thr Glu Glu Ala Asn Arg
725 730 735

Thr Thr Met Glu Val Gln Gln Ala Thr Ala Pro Met Ala Asn Asn Leu
740 745 750

Thr Asn Trp Ser Gln Asn Leu Gln His Phe Asp Ser Ser Ala Tyr Asn
755 760 765

Thr Ala Val Asn Ser Ala Arg Asp Ala Val Arg Asn Leu Thr Glu Val
770 775 780

Val Pro Gln Leu Leu Asp Gln Leu Arg Thr Val Glu Gln Lys Arg Pro
785 790 795 800

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Ala Ser Asn Val Ser Ala Ser Ile Gln Arg Ile Arg Glu Leu Ile Ala
                805                 810                 815

Gln Thr Arg Ser Val Ala Ser Lys Ile Gln Val Ser Met Met Phe Asp
            820                 825                 830

Gly Gln Ser Ala Val Glu Val His Ser Arg Thr Ser Met Asp Asp Leu
        835                 840                 845

Lys Ala Phe Thr Ser Leu Ser Leu Tyr Met Lys Pro Pro Val Lys Arg
    850                 855                 860

Pro Glu Leu Thr Glu Thr Ala Asp Gln Phe Ile Leu Tyr Leu Gly Ser
865                 870                 875                 880

Lys Asn Ala Lys Lys Glu Tyr Met Gly Leu Ala Ile Lys Asn Asp Asn
                885                 890                 895

Leu Val Tyr Val Tyr Asn Leu Gly Thr Lys Asp Val Glu Ile Pro Leu
            900                 905                 910

Asp Ser Lys Pro Val Ser Ser Trp Pro Ala Tyr Phe Ser Ile Val Lys
        915                 920                 925

Ile Glu Arg Val Gly Lys His Gly Lys Val Phe Leu Thr Val Pro Ser
    930                 935                 940

Leu Ser Ser Thr Ala Glu Glu Lys Phe Ile Lys Lys Gly Glu Phe Ser
945                 950                 955                 960

Gly Asp Asp Ser Leu Leu Asp Leu Asp Pro Glu Asp Thr Val Phe Tyr
                965                 970                 975

Val Gly Gly Val Pro Ser Asn Phe Lys Leu Pro Thr Ser Leu Asn Leu
            980                 985                 990

Pro Gly Phe Val Gly Cys Leu Glu Leu Ala Thr Leu Asn Asn Asp Val
        995                1000                1005

Ile Ser Leu Tyr Asn Phe Lys His Ile Tyr Asn Met Asp Pro Ser Thr
   1010                1015                1020

Ser Val Pro Cys Ala Arg Asp Lys Leu Ala Phe Thr Gln Ser Arg Ala
025                1030                1035                1040

Ala Ser Tyr Phe Phe Asp Gly Ser Gly Tyr Ala Val Val Arg Asp Ile
               1045                1050                1055

Pro Arg Arg Gly Lys Phe Gly Gln Val Thr Arg Phe Asp Ile Glu Val
           1060                1065                1070

Arg Thr Pro Ala Asp Asn Gly Leu Ile Leu Leu Met Val Asn Gly Ser
       1075                1080                1085

Met Phe Phe Arg Leu Glu Met Arg Asn Gly Tyr Leu His Val Phe Tyr
   1090                1095                1100

Asp Phe Gly Phe Ser Ser Gly Arg Val His Leu Glu Asp Thr Leu Lys
105                1110                1115                1120

Lys Ala Gln Ile Asn Asp Ala Lys Tyr His Glu Ile Ser Ile Ile Tyr
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1125 1130 1135

His Asn Asp Lys Lys Met Ile Leu Val Val Asp Arg Arg His Val Lys
1140 1145 1150

Ser Met Asp Asn Glu Lys Met Lys Ile Pro Phe Thr Asp Ile Tyr Ile
1155 1160 1165

Gly Gly Ala Pro Pro Glu Ile Leu Gln Ser Arg Ala Leu Arg Ala His
1170 1175 1180

Leu Pro Leu Asp Ile Asn Phe Arg Gly Cys Met Lys Gly Phe Gln Phe
185 1190 1195 1200

Gln Lys Lys Asp Phe Asn Leu Leu Glu Gln Thr Glu Thr Leu Gly Val
1205 1210 1215

Gly Tyr Gly Cys Pro Glu Asp Ser Leu Ile Ser Arg Arg Ala Tyr Phe
1220 1225 1230

Asn Gly Gln Ser Phe Ile Ala Ser Ile Gln Lys Ile Ser Phe Phe Asp
1235 1240 1245

Gly Phe Glu Gly Gly Phe Asn Phe Arg Thr Leu Gln Pro Asn Gly Leu
1250 1255 1260

Leu Phe Tyr Tyr Ala Ser Gly Ser Asp Val Phe Ser Ile Ser Leu Asp
265 1270 1275 1280

Asn Gly Thr Val Ile Met Asp Val Lys Gly Ile Lys Val Gln Ser Val
1285 1290 1295

Asp Lys Gln Tyr Asn Asp Gly Leu Ser His Phe Val Ile Ser Ser Val
1300 1305 1310

Ser Pro Thr Arg Tyr Glu Leu Ile Val Asp Lys Ser Arg Val Gly Ser
1315 1320 1325

Lys Asn Pro Thr Lys Gly Lys Ile Glu Gln Thr Gln Ala Ser Glu Lys
1330 1335 1340

Lys Phe Tyr Phe Gly Gly Ser Pro Ile Ser Ala Gln Tyr Ala Asn Phe
345 1350 1355 1360

Thr Gly Cys Ile Ser Asn Ala Tyr Phe Thr Arg Val Asp Arg Asp Val
1365 1370 1375

Glu Val Glu Asp Phe Gln Arg Tyr Thr Glu Lys Val His Thr Ser Leu
1380 1385 1390

Tyr Glu Cys Pro Ile Glu Ser Ser Pro Leu Phe Leu Leu His Lys Lys
1395 1400 1405

Gly Lys Asn Leu Ser Lys Pro Lys Ala Ser Gln Asn Lys Lys Gly Gly
1410 1415 1420

Lys Ser Lys Asp Ala Pro Ser Trp Asp Pro Val Ala Leu Lys Leu Pro
425 1430 1435 1440

Glu Arg Asn Thr Pro Arg Asn Ser His Cys His Leu Ser Asn Ser Pro
1445 1450 1455

Arg Ala Ile Glu His Ala Tyr Gln Tyr Gly Gly Thr Ala Asn Ser Arg
1460 1465 1470

Gln Glu Phe Glu His Leu Lys Gly Asp Phe Gly Ala Lys Ser Gln Phe
1475 1480 1485

Ser Ile Arg Leu Arg Thr Arg Ser Ser His Gly Met Ile Phe Tyr Val
1490 1495 1500

Ser Asp Gln Glu Glu Asn Asp Phe Met Thr Leu Phe Leu Ala His Gly
505 1510 1515 1520

Arg Leu Val Tyr Met Phe Asn Val Gly His Lys Lys Leu Lys Ile Arg
1525 1530 1535

Ser Gln Glu Lys Tyr Asn Asp Gly Leu Trp His Asp Val Ile Phe Ile
1540 1545 1550

Arg Glu Arg Ser Ser Gly Arg Leu Val Ile Asp Gly Leu Arg Val Leu
1555 1560 1565

Glu Glu Ser Leu Pro Pro Thr Glu Ala Thr Trp Lys Ile Lys Gly Pro
1570 1575 1580

Ile Tyr Leu Gly Gly Val Ala Pro Gly Lys Ala Val Lys Asn Val Gln
585 1590 1595 1600

Ile Asn Ser Ile Tyr Ser Phe Ser Gly Cys Leu Ser Asn Leu Gln Leu
1605 1610 1615

Asn Gly Ala Ser Ile Thr Ser Ala Ser Gln Thr Phe Ser Val Thr Pro
1620 1625 1630

Cys Phe Glu Gly Pro Met Glu Thr Gly Thr Tyr Phe Ser Thr Glu Gly
1635 1640 1645

Gly Tyr Val Val Leu Asp Glu Ser Phe Asn Ile Gly Leu Lys Phe Glu
1650 1655 1660

Ile Ala Phe Glu Val Arg Pro Arg Ser Ser Ser Gly Thr Leu Val His
665 1670 1675 1680

Gly His Ser Val Asn Gly Glu Tyr Leu Asn Val His Met Lys Asn Gly
1685 1690 1695

Gln Val Ile Val Lys Val Asn Asn Gly Ile Arg Asp Phe Ser Thr Ser
1700 1705 1710

Val Thr Pro Lys Gln Ser Leu Cys Asp Gly Arg Trp His Arg Ile Thr
1715 1720 1725

Val Ile Arg Asp Ser Asn Val Val Gln Leu Asp Val Asp Ser Glu Val
1730 1735 1740

Asn His Val Val Gly Pro Leu Asn Pro Lys Pro Ile Asp His Arg Glu
745 1750 1755 1760

Pro Val Phe Val Gly Gly Val Pro Glu Ser Leu Leu Thr Pro Arg Leu
1765 1770 1775

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Ala Pro Ser Lys Pro Phe Thr Gly Cys Ile Arg His Phe Val Ile Asp
          1780                1785                1790

Gly His Pro Val Ser Phe Ser Lys Ala Ala Leu Val Ser Gly Ala Val
       1795                1800                1805

Ser Ile Asn Ser Cys Pro Ala Ala Asp Tyr Lys Asp Asp Asp Asp Lys
   1810                1815                1820
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Ala Ser Gly Asp Asp Asn Ala Phe Pro Phe Asp Ile Glu Gly Ser Ser
  1               5                  10                  15

gcg gtt ggc agg caa gac ccg cct gag acg agc gaa ccc cgc gtg gct   96
Ala Val Gly Arg Gln Asp Pro Pro Glu Thr Ser Glu Pro Arg Val Ala
             20                  25                  30

ctg gga cgc ctg ccg cct gcg gcc gag aaa tgc aat gct gga ttc ttt   144
Leu Gly Arg Leu Pro Pro Ala Ala Glu Lys Cys Asn Ala Gly Phe Phe
         35                  40                  45

cac acc ctg tcg gga gaa tgt gtg ccc tgc gac tgt aat ggc aat tcc   192
His Thr Leu Ser Gly Glu Cys Val Pro Cys Asp Cys Asn Gly Asn Ser
     50                  55                  60

aac gag tgt ttg gac ggc tca gga tac tgt gtg cac tgc cag cgg aac   240
Asn Glu Cys Leu Asp Gly Ser Gly Tyr Cys Val His Cys Gln Arg Asn
 65                  70                  75                  80

aca aca gga gag cac tgt gaa aag tgt ctg gat ggt tat atc gga gat   288
Thr Thr Gly Glu His Cys Glu Lys Cys Leu Asp Gly Tyr Ile Gly Asp
                 85                  90                  95

tcc atc agg gga gca ccc caa ttc tgc cag ccg tgc ccc tgt ccc ctg   336
Ser Ile Arg Gly Ala Pro Gln Phe Cys Gln Pro Cys Pro Cys Pro Leu
            100                 105                 110

ccc cac ttg gcc aat ttt cca gaa tcc tgc tat agg aaa aat gga gct   384
Pro His Leu Ala Asn Phe Pro Glu Ser Cys Tyr Arg Lys Asn Gly Ala
        115                 120                 125

gtt cgg tgc att tgt aac gaa aat tat gct gga cct aac tgt gaa aga   432
Val Arg Cys Ile Cys Asn Glu Asn Tyr Ala Gly Pro Asn Cys Glu Arg
    130                 135                 140

tgt gct ccc ggt tac tat gga aac ccc ttc ctc att gga agc acc tgt   480
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Cys Ala Pro Gly Tyr Tyr Gly Asn Pro Phe Leu Ile Gly Ser Thr Cys
145                 150                 155                 160

aag aaa tgt gac tgc agt gga aat tca gat ccc aac ctg atc ttt gaa   528
Lys Lys Cys Asp Cys Ser Gly Asn Ser Asp Pro Asn Leu Ile Phe Glu
                165                 170                 175

gat tgt gat gaa gtc act ggc cag tgt agg aat tgc tta cgc aac acc   576
Asp Cys Asp Glu Val Thr Gly Gln Cys Arg Asn Cys Leu Arg Asn Thr
            180                 185                 190

acc gga ttc aag tgt gaa cgt tgc gct cct ggc tac tat ggg gac gcc   624
Thr Gly Phe Lys Cys Glu Arg Cys Ala Pro Gly Tyr Tyr Gly Asp Ala
        195                 200                 205

agg ata gcc aag aac tgt gca gtg tgc aac tgc ggg gga ggc cca tgt   672
Arg Ile Ala Lys Asn Cys Ala Val Cys Asn Cys Gly Gly Gly Pro Cys
    210                 215                 220

gac agt gta acc gga gaa tgc ttg gaa gaa ggt ttt gaa ccc cct aca   720
Asp Ser Val Thr Gly Glu Cys Leu Glu Glu Gly Phe Glu Pro Pro Thr
225                 230                 235                 240

ggc tgt gat aag tgc gtc tgg gac ctg act gat gac ctg cgg tta gca   768
Gly Cys Asp Lys Cys Val Trp Asp Leu Thr Asp Asp Leu Arg Leu Ala
                245                 250                 255

gcg ctc tcc atc gag gaa ggc aaa tcc ggg gtg ctg agc gta tcc tct   816
Ala Leu Ser Ile Glu Glu Gly Lys Ser Gly Val Leu Ser Val Ser Ser
            260                 265                 270

ggg gcc gcc gct cat agg cac gtg aat gaa atc aac gcc acc atc tac   864
Gly Ala Ala Ala His Arg His Val Asn Glu Ile Asn Ala Thr Ile Tyr
        275                 280                 285

ctc ctc aaa aca aaa ttg tca gaa aga gaa aac caa tac gcc cta aga   912
Leu Leu Lys Thr Lys Leu Ser Glu Arg Glu Asn Gln Tyr Ala Leu Arg
    290                 295                 300

aag ata caa atc aac aat gct gag aac acg atg aaa agc ctt ctg tct   960
Lys Ile Gln Ile Asn Asn Ala Glu Asn Thr Met Lys Ser Leu Leu Ser
305                 310                 315                 320

gac gta gag gaa tta gtt gaa aag gaa aat caa gcc tcc aga aaa gga   1008
Asp Val Glu Glu Leu Val Glu Lys Glu Asn Gln Ala Ser Arg Lys Gly
                325                 330                 335

caa ctt gtt cag aag gaa agc atg gac acc att aac cac gca agt cag   1056
Gln Leu Val Gln Lys Glu Ser Met Asp Thr Ile Asn His Ala Ser Gln
            340                 345                 350

ctg gta gag caa gcc cat gat atg agg gat aaa atc caa gag atc aac   1104
Leu Val Glu Gln Ala His Asp Met Arg Asp Lys Ile Gln Glu Ile Asn
        355                 360                 365

aac aag atg ctc tat tat ggg gaa gag cat gaa ctt agc ccc aag gaa   1152
Asn Lys Met Leu Tyr Tyr Gly Glu Glu His Glu Leu Ser Pro Lys Glu
    370                 375                 380

atc tct gag aag ctg gtg ttg gcc cag aag atg ctt gaa gag att aga   1200
Ile Ser Glu Lys Leu Val Leu Ala Gln Lys Met Leu Glu Glu Ile Arg
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385                 390                 395                 400

agc cgt caa cca ttt ttc acc caa cgg gag ctc gtg gat gag gag gca   1248
Ser Arg Gln Pro Phe Phe Thr Gln Arg Glu Leu Val Asp Glu Glu Ala
                405                 410                 415

gat gag gct tac gaa cta ctg agc cag gct gag agc tgg cag cgg ctg   1296
Asp Glu Ala Tyr Glu Leu Leu Ser Gln Ala Glu Ser Trp Gln Arg Leu
            420                 425                 430

cac aat gag acc cgc act ctg ttt cct gtc gtc ctg gag cag ctg gat   1344
His Asn Glu Thr Arg Thr Leu Phe Pro Val Val Leu Glu Gln Leu Asp
        435                 440                 445

gac tac aat gct aag ttg tca gat ctc cag gaa gca ctt gac cag gcc   1392
Asp Tyr Asn Ala Lys Leu Ser Asp Leu Gln Glu Ala Leu Asp Gln Ala
    450                 455                 460

ctt aac tat gtc agg gat gcc gaa gac atg aac agg gcc aca gca gcc   1440
Leu Asn Tyr Val Arg Asp Ala Glu Asp Met Asn Arg Ala Thr Ala Ala
465                 470                 475                 480

agg cag cgg gac cat gag aaa caa cag gaa aga gtg agg gaa caa atg   1488
Arg Gln Arg Asp His Glu Lys Gln Gln Glu Arg Val Arg Glu Gln Met
                485                 490                 495

gaa gtg gtg aac atg tct ctg agc aca tct gcg gac tct ctg aca aca   1536
Glu Val Val Asn Met Ser Leu Ser Thr Ser Ala Asp Ser Leu Thr Thr
            500                 505                 510

cct cgt cta act ctt tca gaa ctt gat gat ata ata aag aat gcg tca   1584
Pro Arg Leu Thr Leu Ser Glu Leu Asp Asp Ile Ile Lys Asn Ala Ser
        515                 520                 525

ggg att tat gca gaa ata gat gga gcc aaa agt gaa cta caa gta aaa   1632
Gly Ile Tyr Ala Glu Ile Asp Gly Ala Lys Ser Glu Leu Gln Val Lys
    530                 535                 540

cta tct aac cta agt aac ctc agc cat gat tta gtc caa gaa gct att   1680
Leu Ser Asn Leu Ser Asn Leu Ser His Asp Leu Val Gln Glu Ala Ile
545                 550                 555                 560

gac cat gca cag gac ctt caa caa gaa gct aat gaa ttg agc agg aag   1728
Asp His Ala Gln Asp Leu Gln Gln Glu Ala Asn Glu Leu Ser Arg Lys
                565                 570                 575

ttg cac agt tca gat atg aac ggg ctg gta cag aag gct ttg gat gca   1776
Leu His Ser Ser Asp Met Asn Gly Leu Val Gln Lys Ala Leu Asp Ala
            580                 585                 590

tca aat gtc tat gaa aat att gtt aat tat gtt agt gaa gcc aat gaa   1824
Ser Asn Val Tyr Glu Asn Ile Val Asn Tyr Val Ser Glu Ala Asn Glu
        595                 600                 605

aca gca gaa ttt gct ttg aac acc act gac cga att tat gat gcg gtg   1872
Thr Ala Glu Phe Ala Leu Asn Thr Thr Asp Arg Ile Tyr Asp Ala Val
    610                 615                 620

agt ggg att gat act caa atc att tac cat aaa gat gaa agt gag aac   1920
Ser Gly Ile Asp Thr Gln Ile Ile Tyr His Lys Asp Glu Ser Glu Asn
625                 630                 635                 640
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ctc ctc aat caa gcc aga gaa ctg caa gca aag gca gag tct agc agt   1968
Leu Leu Asn Gln Ala Arg Glu Leu Gln Ala Lys Ala Glu Ser Ser Ser
                645                 650                 655

gat gaa gca gtg gct gac act agc agg cgt gtg ggt gga gcc cta gca   2016
Asp Glu Ala Val Ala Asp Thr Ser Arg Arg Val Gly Gly Ala Leu Ala
            660                 665                 670

agg aaa agt gcc ctt aaa acc aga ctc agt gat gcc gtt aag caa cta   2064
Arg Lys Ser Ala Leu Lys Thr Arg Leu Ser Asp Ala Val Lys Gln Leu
        675                 680                 685

caa gca gca gag aga ggg gat gcc cag cag cgc ctg ggg cag tct aga   2112
Gln Ala Ala Glu Arg Gly Asp Ala Gln Gln Arg Leu Gly Gln Ser Arg
    690                 695                 700

ctg atc acc gag gaa gcc aac agg acg acg atg gag gtg cag cag gcc   2160
Leu Ile Thr Glu Glu Ala Asn Arg Thr Thr Met Glu Val Gln Gln Ala
705                 710                 715                 720

act gcc ccc atg gcc aac aat cta acc aac tgg tca cag aat ctt caa   2208
Thr Ala Pro Met Ala Asn Asn Leu Thr Asn Trp Ser Gln Asn Leu Gln
                725                 730                 735

cat ttt gac tct tct gct tac aac act gca gtg aac tct gct agg gat   2256
His Phe Asp Ser Ser Ala Tyr Asn Thr Ala Val Asn Ser Ala Arg Asp
            740                 745                 750

gca gta aga aat ctg acc gag gtt gtc cct cag ctc ctg gat cag ctt   2304
Ala Val Arg Asn Leu Thr Glu Val Val Pro Gln Leu Leu Asp Gln Leu
        755                 760                 765

cgt acg gtt gag cag aag cga cct gca agc aac gtt tct gcc agc atc   2352
Arg Thr Val Glu Gln Lys Arg Pro Ala Ser Asn Val Ser Ala Ser Ile
    770                 775                 780

cag agg atc cga gag ctc att gct cag acc aga agt gtt gcc agc aag   2400
Gln Arg Ile Arg Glu Leu Ile Ala Gln Thr Arg Ser Val Ala Ser Lys
785                 790                 795                 800

atc caa gtc tcc atg atg ttt gat ggc cag tca gct gtg gaa gtg cac   2448
Ile Gln Val Ser Met Met Phe Asp Gly Gln Ser Ala Val Glu Val His
                805                 810                 815

tcg aga acc agt atg gat gac tta aag gcc ttc acg tct ctg agc ctg   2496
Ser Arg Thr Ser Met Asp Asp Leu Lys Ala Phe Thr Ser Leu Ser Leu
            820                 825                 830

tac atg aaa ccc cct gtg aag cgg ccg gaa ctg acc gag act gca gat   2544
Tyr Met Lys Pro Pro Val Lys Arg Pro Glu Leu Thr Glu Thr Ala Asp
        835                 840                 845

cag ttt atc ctg tac ctc gga agc aaa aac gcc aaa aaa gag tat atg   2592
Gln Phe Ile Leu Tyr Leu Gly Ser Lys Asn Ala Lys Lys Glu Tyr Met
    850                 855                 860

ggt ctt gca atc aaa aat gat aat ctg gta tac gtc tat aat ttg gga   2640
Gly Leu Ala Ile Lys Asn Asp Asn Leu Val Tyr Val Tyr Asn Leu Gly
865                 870                 875                 880
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act aaa gat gtg gag att ccc ctg gac tcc aag ccc gtc agt tcc tgg   2688
Thr Lys Asp Val Glu Ile Pro Leu Asp Ser Lys Pro Val Ser Ser Trp
                885                 890                 895

cct gct tac ttc agc att gtc aag att gaa agg gtg gga aaa cat gga   2736
Pro Ala Tyr Phe Ser Ile Val Lys Ile Glu Arg Val Gly Lys His Gly
            900                 905                 910

aag gtg ttt tta aca gtc ccg agt cta agt agc aca gca gag gaa aag   2784
Lys Val Phe Leu Thr Val Pro Ser Leu Ser Ser Thr Ala Glu Glu Lys
        915                 920                 925

ttc att aaa aag ggg gaa ttt tcg gga gat gac tct ctg ctg gac ctg   2832
Phe Ile Lys Lys Gly Glu Phe Ser Gly Asp Asp Ser Leu Leu Asp Leu
    930                 935                 940

gac cct gag gac aca gtg ttt tat gtt ggt gga gtg cct tcc aac ttc   2880
Asp Pro Glu Asp Thr Val Phe Tyr Val Gly Gly Val Pro Ser Asn Phe
945                 950                 955                 960

aag ctc cct acc agc tta aac ctg cct ggc ttt gtt ggc tgc ctg gaa   2928
Lys Leu Pro Thr Ser Leu Asn Leu Pro Gly Phe Val Gly Cys Leu Glu
                965                 970                 975

ctg gcc act ttg aat aat gat gtg atc agc ttg tac aac ttt aag cac   2976
Leu Ala Thr Leu Asn Asn Asp Val Ile Ser Leu Tyr Asn Phe Lys His
            980                 985                 990

atc tat aat atg gac ccc tcc aca tca gtg cca tgt gcc cga gat aag   3024
Ile Tyr Asn Met Asp Pro Ser Thr Ser Val Pro Cys Ala Arg Asp Lys
        995                1000                1005

ctg gcc ttc act cag agt cgg gct gcc agt tac ttc ttc gat ggc tcc   3072
Leu Ala Phe Thr Gln Ser Arg Ala Ala Ser Tyr Phe Phe Asp Gly Ser
   1010                1015                1020

ggt tat gcc gtg gtg aga gac ata cca agg aga ggg aaa ttt ggt cag   3120
Gly Tyr Ala Val Val Arg Asp Ile Pro Arg Arg Gly Lys Phe Gly Gln
1025                1030                1035                1040

gtg act cgc ttt gac ata gaa gtt cga aca cca gct gac aac ggc ctt   3168
Val Thr Arg Phe Asp Ile Glu Val Arg Thr Pro Ala Asp Asn Gly Leu
                1045                1050                1055

att ctc ctg atg gtc aat gga agt atg ttt ttc aga ctg gaa atg cgc   3216
Ile Leu Leu Met Val Asn Gly Ser Met Phe Phe Arg Leu Glu Met Arg
            1060                1065                1070

aat ggt tac cta cat gtg ttc tat gat ttt gga ttc agc agt ggc cgt   3264
Asn Gly Tyr Leu His Val Phe Tyr Asp Phe Gly Phe Ser Ser Gly Arg
        1075                1080                1085

gtg cat ctt gaa gat acg tta aag aaa gct caa att aat gat gca aaa   3312
Val His Leu Glu Asp Thr Leu Lys Lys Ala Gln Ile Asn Asp Ala Lys
   1090                1095                1100

tac cat gag atc tca atc att tac cac aat gat aag aaa atg atc ttg   3360
Tyr His Glu Ile Ser Ile Ile Tyr His Asn Asp Lys Lys Met Ile Leu
1105                1110                1115                1120

gta gtt gac aga agg cat gtc aag agc atg gat aat gaa aag atg aaa   3408
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Val Val Asp Arg Arg His Val Lys Ser Met Asp Asn Glu Lys Met Lys
                1125                1130                1135

ata cct ttt aca gat ata tac att gga gga gct cct cca gaa atc tta   3456
Ile Pro Phe Thr Asp Ile Tyr Ile Gly Gly Ala Pro Pro Glu Ile Leu
            1140                1145                1150

caa tcc agg gcc ctc aga gca cac ctt ccc cta gat atc aac ttc aga   3504
Gln Ser Arg Ala Leu Arg Ala His Leu Pro Leu Asp Ile Asn Phe Arg
        1155                1160                1165

gga tgc atg aag ggc ttc cag ttc caa aag aag gac ttc aat tta ctg   3552
Gly Cys Met Lys Gly Phe Gln Phe Gln Lys Lys Asp Phe Asn Leu Leu
    1170                1175                1180

gag cag aca gaa acc ctg gga gtt ggt tat gga tgc cca gaa gac tca   3600
Glu Gln Thr Glu Thr Leu Gly Val Gly Tyr Gly Cys Pro Glu Asp Ser
1185                1190                1195                1200

ctt ata tct cgc aga gca tat ttc aat gga cag agc ttc att gct tca   3648
Leu Ile Ser Arg Arg Ala Tyr Phe Asn Gly Gln Ser Phe Ile Ala Ser
                1205                1210                1215

att cag aaa ata tct ttc ttt gat ggc ttt gaa gga ggt ttt aat ttc   3696
Ile Gln Lys Ile Ser Phe Phe Asp Gly Phe Glu Gly Gly Phe Asn Phe
            1220                1225                1230

cga aca tta caa cca aat ggg tta cta ttc tat tat gct tca ggg tca   3744
Arg Thr Leu Gln Pro Asn Gly Leu Leu Phe Tyr Tyr Ala Ser Gly Ser
        1235                1240                1245

gac gtg ttc tcc atc tca ctg gat aat ggt act gtc atc atg gat gta   3792
Asp Val Phe Ser Ile Ser Leu Asp Asn Gly Thr Val Ile Met Asp Val
    1250                1255                1260

aag gga atc aaa gtt cag tca gta gat aag cag tac aat gat ggg ctg   3840
Lys Gly Ile Lys Val Gln Ser Val Asp Lys Gln Tyr Asn Asp Gly Leu
1265                1270                1275                1280

tcc cac ttc gtc att agc tct gtc tca ccc aca aga tat gaa ctg ata   3888
Ser His Phe Val Ile Ser Ser Val Ser Pro Thr Arg Tyr Glu Leu Ile
                1285                1290                1295

gta gat aaa agc aga gtt ggg agt aag aat cct acc aaa ggg aaa ata   3936
Val Asp Lys Ser Arg Val Gly Ser Lys Asn Pro Thr Lys Gly Lys Ile
            1300                1305                1310

gaa cag aca caa gca agt gaa aag aag ttt tac ttc ggt ggc tca cca   3984
Glu Gln Thr Gln Ala Ser Glu Lys Lys Phe Tyr Phe Gly Gly Ser Pro
        1315                1320                1325

atc agt gct cag tat gct aat ttc act ggc tgc ata agt aat gcc tac   4032
Ile Ser Ala Gln Tyr Ala Asn Phe Thr Gly Cys Ile Ser Asn Ala Tyr
    1330                1335                1340

ttt acc agg gtg gat aga gat gtg gag gtt gaa gat ttc caa cgg tat   4080
Phe Thr Arg Val Asp Arg Asp Val Glu Val Glu Asp Phe Gln Arg Tyr
1345                1350                1355                1360

act gaa aag gtc cac act tct ctt tat gag tgt ccc att gag tct tca   4128
Thr Glu Lys Val His Thr Ser Leu Tyr Glu Cys Pro Ile Glu Ser Ser
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                1365                1370                1375

cca ttg ttt ctc ctc cat aaa aaa gga aaa aat tta tcc aag cct aaa   4176
Pro Leu Phe Leu Leu His Lys Lys Gly Lys Asn Leu Ser Lys Pro Lys
            1380                1385                1390

gca agt cag aat aaa aag gga ggg aaa agt aaa gat gca cct tca tgg   4224
Ala Ser Gln Asn Lys Lys Gly Gly Lys Ser Lys Asp Ala Pro Ser Trp
        1395                1400                1405

gat cct gtt gct ctg aaa ctc cca gag cgg aat act cca aga aac tct   4272
Asp Pro Val Ala Leu Lys Leu Pro Glu Arg Asn Thr Pro Arg Asn Ser
    1410                1415                1420

cat tgc cac ctt tcc aac agc cct aga gca ata gag cac gcc tat caa   4320
His Cys His Leu Ser Asn Ser Pro Arg Ala Ile Glu His Ala Tyr Gln
1425                1430                1435                1440

tat gga gga aca gcc aac agc cgc caa gag ttt gaa cac tta aaa gga   4368
Tyr Gly Gly Thr Ala Asn Ser Arg Gln Glu Phe Glu His Leu Lys Gly
                1445                1450                1455

gat ttt ggt gcc aaa tct cag ttt tcc att cgt ctg aga act cgt tcc   4416
Asp Phe Gly Ala Lys Ser Gln Phe Ser Ile Arg Leu Arg Thr Arg Ser
            1460                1465                1470

tcc cat ggc atg atc ttc tat gtc tca gat caa gaa gag aat gac ttc   4464
Ser His Gly Met Ile Phe Tyr Val Ser Asp Gln Glu Glu Asn Asp Phe
        1475                1480                1485

atg act cta ttt ttg gcc cat ggc cgc ttg gtt tac atg ttt aat gtt   4512
Met Thr Leu Phe Leu Ala His Gly Arg Leu Val Tyr Met Phe Asn Val
    1490                1495                1500

ggt cac aaa aaa ctg aag att aga agc cag gag aaa tac aat gat ggc   4560
Gly His Lys Lys Leu Lys Ile Arg Ser Gln Glu Lys Tyr Asn Asp Gly
1505                1510                1515                1520

ctg tgg cat gat gtg ata ttt att cga gaa agg agc agt ggc cga ctg   4608
Leu Trp His Asp Val Ile Phe Ile Arg Glu Arg Ser Ser Gly Arg Leu
                1525                1530                1535

gta att gat ggt ctc cga gtc cta gaa gaa agt ctt cct cct act gaa   4656
Val Ile Asp Gly Leu Arg Val Leu Glu Glu Ser Leu Pro Pro Thr Glu
            1540                1545                1550

gct acc tgg aaa atc aag ggt ccc att tat ttg gga ggt gtg gct cct   4704
Ala Thr Trp Lys Ile Lys Gly Pro Ile Tyr Leu Gly Gly Val Ala Pro
        1555                1560                1565

gga aag gct gtg aaa aat gtt cag att aac tcc atc tac agt ttt agt   4752
Gly Lys Ala Val Lys Asn Val Gln Ile Asn Ser Ile Tyr Ser Phe Ser
    1570                1575                1580

ggc tgt ctc agc aat ctc cag ctc aat ggg gcc tcc atc acc tct gct   4800
Gly Cys Leu Ser Asn Leu Gln Leu Asn Gly Ala Ser Ile Thr Ser Ala
1585                1590                1595                1600

tct cag aca ttc agt gtg acc cct tgc ttt gaa ggc ccc atg gaa aca   4848
Ser Gln Thr Phe Ser Val Thr Pro Cys Phe Glu Gly Pro Met Glu Thr
                1605                1610                1615
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gga act tac ttt tca aca gaa gga gga tac gtg gtt cta gat gaa tct   4896
Gly Thr Tyr Phe Ser Thr Glu Gly Gly Tyr Val Val Leu Asp Glu Ser
          1620                1625                1630

ttc aat att gga ttg aag ttt gaa att gca ttt gaa gtc cgt ccc aga   4944
Phe Asn Ile Gly Leu Lys Phe Glu Ile Ala Phe Glu Val Arg Pro Arg
      1635                1640                1645

agc agt tcc gga acc ctg gtc cac ggc cac agt gtc aat ggg gag tac   4992
Ser Ser Ser Gly Thr Leu Val His Gly His Ser Val Asn Gly Glu Tyr
   1650                1655                1660

cta aat gtt cac atg aaa aat gga cag gtc ata gtg aaa gtc aat aat   5040
Leu Asn Val His Met Lys Asn Gly Gln Val Ile Val Lys Val Asn Asn
1665                1670                1675                1680

ggc atc aga gat ttt tcc acc tca gta aca ccc aag cag agt ctc tgt   5088
Gly Ile Arg Asp Phe Ser Thr Ser Val Thr Pro Lys Gln Ser Leu Cys
               1685                1690                1695

gat ggc aga tgg cac aga att aca gtt att aga gat tct aat gtg gtt   5136
Asp Gly Arg Trp His Arg Ile Thr Val Ile Arg Asp Ser Asn Val Val
          1700                1705                1710

cag ttg gat gtg gac tct gaa gtg aac cat gtg gtt gga ccc ctg aat   5184
Gln Leu Asp Val Asp Ser Glu Val Asn His Val Val Gly Pro Leu Asn
      1715                1720                1725

cca aaa cca att gat cac agg gag cct gtg ttt gtt gga ggt gtt cca   5232
Pro Lys Pro Ile Asp His Arg Glu Pro Val Phe Val Gly Gly Val Pro
   1730                1735                1740

gaa tct cta ctg aca cca cgc ttg gcc ccc agc aaa ccc ttc aca ggc   5280
Glu Ser Leu Leu Thr Pro Arg Leu Ala Pro Ser Lys Pro Phe Thr Gly
1745                1750                1755                1760

tgc ata cgc cac ttt gtg att gat gga cac cca gtg agc ttc agt aaa   5328
Cys Ile Arg His Phe Val Ile Asp Gly His Pro Val Ser Phe Ser Lys
               1765                1770                1775

gca gcc ctg gtc agc ggc gcc gta agc atc aac tcc tgt cca gca gcc   5376
Ala Ala Leu Val Ser Gly Ala Val Ser Ile Asn Ser Cys Pro Ala Ala
          1780                1785                1790

gac tac aag gac gac gat gac aag taagcttggc                       5410
Asp Tyr Lys Asp Asp Asp Asp Lys
      1795                1800
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<210> 8
<211> 1800
<212> PRT
<213> Homo sapiens

<400> 8

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Ala Ser Gly Asp Asp Asn Ala Phe Pro Phe Asp Ile Glu Gly Ser Ser
  1               5                  10                  15

Ala Val Gly Arg Gln Asp Pro Pro Glu Thr Ser Glu Pro Arg Val Ala
             20                  25                  30
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Leu Gly Arg Leu Pro Pro Ala Ala Glu Lys Cys Asn Ala Gly Phe Phe
         35                  40                  45

His Thr Leu Ser Gly Glu Cys Val Pro Cys Asp Cys Asn Gly Asn Ser
     50                  55                  60

Asn Glu Cys Leu Asp Gly Ser Gly Tyr Cys Val His Cys Gln Arg Asn
 65                  70                  75                  80

Thr Thr Gly Glu His Cys Glu Lys Cys Leu Asp Gly Tyr Ile Gly Asp
                 85                  90                  95

Ser Ile Arg Gly Ala Pro Gln Phe Cys Gln Pro Cys Pro Cys Pro Leu
            100                 105                 110

Pro His Leu Ala Asn Phe Pro Glu Ser Cys Tyr Arg Lys Asn Gly Ala
        115                 120                 125

Val Arg Cys Ile Cys Asn Glu Asn Tyr Ala Gly Pro Asn Cys Glu Arg
    130                 135                 140

Cys Ala Pro Gly Tyr Tyr Gly Asn Pro Phe Leu Ile Gly Ser Thr Cys
145                 150                 155                 160

Lys Lys Cys Asp Cys Ser Gly Asn Ser Asp Pro Asn Leu Ile Phe Glu
                165                 170                 175

Asp Cys Asp Glu Val Thr Gly Gln Cys Arg Asn Cys Leu Arg Asn Thr
            180                 185                 190

Thr Gly Phe Lys Cys Glu Arg Cys Ala Pro Gly Tyr Tyr Gly Asp Ala
        195                 200                 205

Arg Ile Ala Lys Asn Cys Ala Val Cys Asn Cys Gly Gly Gly Pro Cys
    210                 215                 220

Asp Ser Val Thr Gly Glu Cys Leu Glu Glu Gly Phe Glu Pro Pro Thr
225                 230                 235                 240

Gly Cys Asp Lys Cys Val Trp Asp Leu Thr Asp Asp Leu Arg Leu Ala
                245                 250                 255

Ala Leu Ser Ile Glu Glu Gly Lys Ser Gly Val Leu Ser Val Ser Ser
            260                 265                 270

Gly Ala Ala Ala His Arg His Val Asn Glu Ile Asn Ala Thr Ile Tyr
        275                 280                 285

Leu Leu Lys Thr Lys Leu Ser Glu Arg Glu Asn Gln Tyr Ala Leu Arg
    290                 295                 300

Lys Ile Gln Ile Asn Asn Ala Glu Asn Thr Met Lys Ser Leu Leu Ser
305                 310                 315                 320

Asp Val Glu Glu Leu Val Glu Lys Glu Asn Gln Ala Ser Arg Lys Gly
                325                 330                 335

Gln Leu Val Gln Lys Glu Ser Met Asp Thr Ile Asn His Ala Ser Gln
            340                 345                 350
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Leu Val Glu Gln Ala His Asp Met Arg Asp Lys Ile Gln Glu Ile Asn
        355                 360                 365

Asn Lys Met Leu Tyr Tyr Gly Glu Glu His Glu Leu Ser Pro Lys Glu
    370                 375                 380

Ile Ser Glu Lys Leu Val Leu Ala Gln Lys Met Leu Glu Glu Ile Arg
385                 390                 395                 400

Ser Arg Gln Pro Phe Phe Thr Gln Arg Glu Leu Val Asp Glu Glu Ala
                405                 410                 415

Asp Glu Ala Tyr Glu Leu Leu Ser Gln Ala Glu Ser Trp Gln Arg Leu
            420                 425                 430

His Asn Glu Thr Arg Thr Leu Phe Pro Val Val Leu Glu Gln Leu Asp
        435                 440                 445

Asp Tyr Asn Ala Lys Leu Ser Asp Leu Gln Glu Ala Leu Asp Gln Ala
    450                 455                 460

Leu Asn Tyr Val Arg Asp Ala Glu Asp Met Asn Arg Ala Thr Ala Ala
465                 470                 475                 480

Arg Gln Arg Asp His Glu Lys Gln Gln Glu Arg Val Arg Glu Gln Met
                485                 490                 495

Glu Val Val Asn Met Ser Leu Ser Thr Ser Ala Asp Ser Leu Thr Thr
            500                 505                 510

Pro Arg Leu Thr Leu Ser Glu Leu Asp Asp Ile Ile Lys Asn Ala Ser
        515                 520                 525

Gly Ile Tyr Ala Glu Ile Asp Gly Ala Lys Ser Glu Leu Gln Val Lys
    530                 535                 540

Leu Ser Asn Leu Ser Asn Leu Ser His Asp Leu Val Gln Glu Ala Ile
545                 550                 555                 560

Asp His Ala Gln Asp Leu Gln Gln Glu Ala Asn Glu Leu Ser Arg Lys
                565                 570                 575

Leu His Ser Ser Asp Met Asn Gly Leu Val Gln Lys Ala Leu Asp Ala
            580                 585                 590

Ser Asn Val Tyr Glu Asn Ile Val Asn Tyr Val Ser Glu Ala Asn Glu
        595                 600                 605

Thr Ala Glu Phe Ala Leu Asn Thr Thr Asp Arg Ile Tyr Asp Ala Val
    610                 615                 620

Ser Gly Ile Asp Thr Gln Ile Ile Tyr His Lys Asp Glu Ser Glu Asn
625                 630                 635                 640

Leu Leu Asn Gln Ala Arg Glu Leu Gln Ala Lys Ala Glu Ser Ser Ser
                645                 650                 655

Asp Glu Ala Val Ala Asp Thr Ser Arg Arg Val Gly Gly Ala Leu Ala
            660                 665                 670

Arg Lys Ser Ala Leu Lys Thr Arg Leu Ser Asp Ala Val Lys Gln Leu
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675 680 685

Gln Ala Ala Glu Arg Gly Asp Ala Gln Gln Arg Leu Gly Gln Ser Arg
690 695 700

Leu Ile Thr Glu Glu Ala Asn Arg Thr Thr Met Glu Val Gln Gln Ala
705 710 715 720

Thr Ala Pro Met Ala Asn Asn Leu Thr Asn Trp Ser Gln Asn Leu Gln
725 730 735

His Phe Asp Ser Ser Ala Tyr Asn Thr Ala Val Asn Ser Ala Arg Asp
740 745 750

Ala Val Arg Asn Leu Thr Glu Val Val Pro Gln Leu Leu Asp Gln Leu
755 760 765

Arg Thr Val Glu Gln Lys Arg Pro Ala Ser Asn Val Ser Ala Ser Ile
770 775 780

Gln Arg Ile Arg Glu Leu Ile Ala Gln Thr Arg Ser Val Ala Ser Lys
785 790 795 800

Ile Gln Val Ser Met Met Phe Asp Gly Gln Ser Ala Val Glu Val His
805 810 815

Ser Arg Thr Ser Met Asp Asp Leu Lys Ala Phe Thr Ser Leu Ser Leu
820 825 830

Tyr Met Lys Pro Pro Val Lys Arg Pro Glu Leu Thr Glu Thr Ala Asp
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Gln Phe Ile Leu Tyr Leu Gly Ser Lys Asn Ala Lys Lys Glu Tyr Met
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Gly Leu Ala Ile Lys Asn Asp Asn Leu Val Tyr Val Tyr Asn Leu Gly
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Thr Lys Asp Val Glu Ile Pro Leu Asp Ser Lys Pro Val Ser Ser Trp
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Pro Ala Tyr Phe Ser Ile Val Lys Ile Glu Arg Val Gly Lys His Gly
900 905 910

Lys Val Phe Leu Thr Val Pro Ser Leu Ser Ser Thr Ala Glu Glu Lys
915 920 925

Phe Ile Lys Lys Gly Glu Phe Ser Gly Asp Asp Ser Leu Leu Asp Leu
930 935 940

Asp Pro Glu Asp Thr Val Phe Tyr Val Gly Gly Val Pro Ser Asn Phe
945 950 955 960

Lys Leu Pro Thr Ser Leu Asn Leu Pro Gly Phe Val Gly Cys Leu Glu
965 970 975

Leu Ala Thr Leu Asn Asn Asp Val Ile Ser Leu Tyr Asn Phe Lys His
980 985 990

Ile Tyr Asn Met Asp Pro Ser Thr Ser Val Pro Cys Ala Arg Asp Lys
995 1000 1005

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Leu Ala Phe Thr Gln Ser Arg Ala Ala Ser Tyr Phe Phe Asp Gly Ser
   1010                1015                1020

Gly Tyr Ala Val Val Arg Asp Ile Pro Arg Arg Gly Lys Phe Gly Gln
1025                1030                1035                1040

Val Thr Arg Phe Asp Ile Glu Val Arg Thr Pro Ala Asp Asn Gly Leu
                1045                1050                1055

Ile Leu Leu Met Val Asn Gly Ser Met Phe Phe Arg Leu Glu Met Arg
            1060                1065                1070

Asn Gly Tyr Leu His Val Phe Tyr Asp Phe Gly Phe Ser Ser Gly Arg
        1075                1080                1085

Val His Leu Glu Asp Thr Leu Lys Lys Ala Gln Ile Asn Asp Ala Lys
   1090                1095                1100

Tyr His Glu Ile Ser Ile Ile Tyr His Asn Asp Lys Lys Met Ile Leu
1105                1110                1115                1120

Val Val Asp Arg Arg His Val Lys Ser Met Asp Asn Glu Lys Met Lys
                1125                1130                1135

Ile Pro Phe Thr Asp Ile Tyr Ile Gly Gly Ala Pro Pro Glu Ile Leu
            1140                1145                1150

Gln Ser Arg Ala Leu Arg Ala His Leu Pro Leu Asp Ile Asn Phe Arg
        1155                1160                1165

Gly Cys Met Lys Gly Phe Gln Phe Gln Lys Lys Asp Phe Asn Leu Leu
   1170                1175                1180

Glu Gln Thr Glu Thr Leu Gly Val Gly Tyr Gly Cys Pro Glu Asp Ser
1185                1190                1195                1200

Leu Ile Ser Arg Arg Ala Tyr Phe Asn Gly Gln Ser Phe Ile Ala Ser
                1205                1210                1215

Ile Gln Lys Ile Ser Phe Phe Asp Gly Phe Glu Gly Gly Phe Asn Phe
            1220                1225                1230

Arg Thr Leu Gln Pro Asn Gly Leu Leu Phe Tyr Tyr Ala Ser Gly Ser
        1235                1240                1245

Asp Val Phe Ser Ile Ser Leu Asp Asn Gly Thr Val Ile Met Asp Val
   1250                1255                1260

Lys Gly Ile Lys Val Gln Ser Val Asp Lys Gln Tyr Asn Asp Gly Leu
1265                1270                1275                1280

Ser His Phe Val Ile Ser Ser Val Ser Pro Thr Arg Tyr Glu Leu Ile
                1285                1290                1295

Val Asp Lys Ser Arg Val Gly Ser Lys Asn Pro Thr Lys Gly Lys Ile
            1300                1305                1310

Glu Gln Thr Gln Ala Ser Glu Lys Lys Phe Tyr Phe Gly Gly Ser Pro
        1315                1320                1325
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Ile Ser Ala Gln Tyr Ala Asn Phe Thr Gly Cys Ile Ser Asn Ala Tyr
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Phe Thr Arg Val Asp Arg Asp Val Glu Val Glu Asp Phe Gln Arg Tyr
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Thr Glu Lys Val His Thr Ser Leu Tyr Glu Cys Pro Ile Glu Ser Ser
                1365                1370                1375

Pro Leu Phe Leu Leu His Lys Lys Gly Lys Asn Leu Ser Lys Pro Lys
            1380                1385                1390

Ala Ser Gln Asn Lys Lys Gly Gly Lys Ser Lys Asp Ala Pro Ser Trp
        1395                1400                1405

Asp Pro Val Ala Leu Lys Leu Pro Glu Arg Asn Thr Pro Arg Asn Ser
   1410                1415                1420

His Cys His Leu Ser Asn Ser Pro Arg Ala Ile Glu His Ala Tyr Gln
1425                1430                1435                1440

Tyr Gly Gly Thr Ala Asn Ser Arg Gln Glu Phe Glu His Leu Lys Gly
                1445                1450                1455

Asp Phe Gly Ala Lys Ser Gln Phe Ser Ile Arg Leu Arg Thr Arg Ser
            1460                1465                1470

Ser His Gly Met Ile Phe Tyr Val Ser Asp Gln Glu Glu Asn Asp Phe
        1475                1480                1485

Met Thr Leu Phe Leu Ala His Gly Arg Leu Val Tyr Met Phe Asn Val
   1490                1495                1500

Gly His Lys Lys Leu Lys Ile Arg Ser Gln Glu Lys Tyr Asn Asp Gly
1505                1510                1515                1520

Leu Trp His Asp Val Ile Phe Ile Arg Glu Arg Ser Ser Gly Arg Leu
                1525                1530                1535

Val Ile Asp Gly Leu Arg Val Leu Glu Glu Ser Leu Pro Pro Thr Glu
            1540                1545                1550

Ala Thr Trp Lys Ile Lys Gly Pro Ile Tyr Leu Gly Gly Val Ala Pro
        1555                1560                1565

Gly Lys Ala Val Lys Asn Val Gln Ile Asn Ser Ile Tyr Ser Phe Ser
   1570                1575                1580

Gly Cys Leu Ser Asn Leu Gln Leu Asn Gly Ala Ser Ile Thr Ser Ala
1585                1590                1595                1600

Ser Gln Thr Phe Ser Val Thr Pro Cys Phe Glu Gly Pro Met Glu Thr
                1605                1610                1615

Gly Thr Tyr Phe Ser Thr Glu Gly Gly Tyr Val Val Leu Asp Glu Ser
            1620                1625                1630

Phe Asn Ile Gly Leu Lys Phe Glu Ile Ala Phe Glu Val Arg Pro Arg
        1635                1640                1645

Ser Ser Ser Gly Thr Leu Val His Gly His Ser Val Asn Gly Glu Tyr
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   1650                1655                1660

Leu Asn Val His Met Lys Asn Gly Gln Val Ile Val Lys Val Asn Asn
1665               1670                1675                1680

Gly Ile Arg Asp Phe Ser Thr Ser Val Thr Pro Lys Gln Ser Leu Cys
               1685                1690                1695

Asp Gly Arg Trp His Arg Ile Thr Val Ile Arg Asp Ser Asn Val Val
           1700                1705                1710

Gln Leu Asp Val Asp Ser Glu Val Asn His Val Val Gly Pro Leu Asn
       1715                1720                1725

Pro Lys Pro Ile Asp His Arg Glu Pro Val Phe Val Gly Gly Val Pro
   1730                1735                1740

Glu Ser Leu Leu Thr Pro Arg Leu Ala Pro Ser Lys Pro Phe Thr Gly
1745               1750                1755                1760

Cys Ile Arg His Phe Val Ile Asp Gly His Pro Val Ser Phe Ser Lys
               1765                1770                1775

Ala Ala Leu Val Ser Gly Ala Val Ser Ile Asn Ser Cys Pro Ala Ala
           1780                1785                1790

Asp Tyr Lys Asp Asp Asp Asp Lys
       1795                1800


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caggcatcac tgcatctctt agggggtacc caccaagacc tccaggtcct tcactccagg 180

aagggccctg ttgaatatct gcagagag atg ggt tgg agc aca gct tgg tgc    232
                                Met Gly Trp Ser Thr Ala Trp Cys
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tca gtc ctg gcc ctg tgg ctc ctc tgg tgt gct gtc tgc tcc aac gca   280
Ser Val Leu Ala Leu Trp Leu Leu Trp Cys Ala Val Cys Ser Asn Ala
     10                  15                  20

gcg tca ggg gac ggc aat gcg ttt cct ttt gac atc gag ggg agc gca   328
Ala Ser Gly Asp Gly Asn Ala Phe Pro Phe Asp Ile Glu Gly Ser Ala
 25                  30                  35                  40
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gtg gtc ggc agg caa gac cca tcg gag act agc gac tca ggc gtg aca   376
Val Val Gly Arg Gln Asp Pro Ser Glu Thr Ser Asp Ser Gly Val Thr
                45                  50                  55

ctg gga cgc ctg ccg cct gct gct gag aga tgt gac gct gga ttc ttc   424
Leu Gly Arg Leu Pro Pro Ala Ala Glu Arg Cys Asp Ala Gly Phe Phe
            60                  65                  70

cgc aca ctg tca gga gaa tgt gca ccc tgt gac tgt aat ggc aat tcc   472
Arg Thr Leu Ser Gly Glu Cys Ala Pro Cys Asp Cys Asn Gly Asn Ser
        75                  80                  85

cat gag tgc ttg gat ggc tcc gga ttc tgt ctg cac tgc cag cgg aac   520
His Glu Cys Leu Asp Gly Ser Gly Phe Cys Leu His Cys Gln Arg Asn
    90                  95                  100

aca aca gga gag cac tgt gaa aaa tgt ctg gat ggc tat att gga gac   568
Thr Thr Gly Glu His Cys Glu Lys Cys Leu Asp Gly Tyr Ile Gly Asp
105                 110                 115                 120

tcc atc aga ggc aca ccc cgg ttc tgc cag ccg tgc ccc tgt ccc ttg   616
Ser Ile Arg Gly Thr Pro Arg Phe Cys Gln Pro Cys Pro Cys Pro Leu
                125                 130                 135

ccc cac ctg gcc aac ttt gca gaa tcc tgc tac agg aaa aat gga gct   664
Pro His Leu Ala Asn Phe Ala Glu Ser Cys Tyr Arg Lys Asn Gly Ala
            140                 145                 150

gtt cgg tgt att tgt aaa gaa aac tat gtt gga cct aac tgt gaa aga   712
Val Arg Cys Ile Cys Lys Glu Asn Tyr Val Gly Pro Asn Cys Glu Arg
        155                 160                 165

tgt gct cct ggt tac tat gga aac ccc tta ctc att gga agc acc tgt   760
Cys Ala Pro Gly Tyr Tyr Gly Asn Pro Leu Leu Ile Gly Ser Thr Cys
    170                 175                 180

aag aaa tgt gac tgc agt gga aat tcg gat ccc aac ctg atc ttt gaa   808
Lys Lys Cys Asp Cys Ser Gly Asn Ser Asp Pro Asn Leu Ile Phe Glu
185                 190                 195                 200

gac tgt gat gaa atc act ggc cag tgc agg aac tgc tta cga aat acc   856
Asp Cys Asp Glu Ile Thr Gly Gln Cys Arg Asn Cys Leu Arg Asn Thr
                205                 210                 215

acc gga ttc aag tgt gaa cgc tgt gca cct ggt tac tat gga gac gcc   904
Thr Gly Phe Lys Cys Glu Arg Cys Ala Pro Gly Tyr Tyr Gly Asp Ala
            220                 225                 230

agg aca gcc aag aac tgt gca gtg tgc aac tgt ggg ggc ggc ccg cgt   952
Arg Thr Ala Lys Asn Cys Ala Val Cys Asn Cys Gly Gly Gly Pro Arg
        235                 240                 245

gac agt gta acc gga gag tgc ttg gaa gaa gga ttt gaa gtc cct aca   1000
Asp Ser Val Thr Gly Glu Cys Leu Glu Glu Gly Phe Glu Val Pro Thr
    250                 255                 260

ggc tgt gat aag tgc gtc tgg gac ttg acc gat gac ctg cga tta gca   1048
Gly Cys Asp Lys Cys Val Trp Asp Leu Thr Asp Asp Leu Arg Leu Ala
265                 270                 275                 280
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gcg ctc tcc atc gaa gag agc aaa tcc ggg ctg ctg agc gtg tcc tct   1096
Ala Leu Ser Ile Glu Glu Ser Lys Ser Gly Leu Leu Ser Val Ser Ser
                285                 290                 295

gcg gct gcg gcg cat aga cac gtg acc gac atg aac tct acc atc cac   1144
Ala Ala Ala Ala His Arg His Val Thr Asp Met Asn Ser Thr Ile His
            300                 305                 310

ctc ctc aga aca agg ctg tca gaa aga gaa aac cag tat acc cta aga   1192
Leu Leu Arg Thr Arg Leu Ser Glu Arg Glu Asn Gln Tyr Thr Leu Arg
        315                 320                 325

aag ata cag ata aac aac tcg gag aac aca ctg aga agc ctc ctg cct   1240
Lys Ile Gln Ile Asn Asn Ser Glu Asn Thr Leu Arg Ser Leu Leu Pro
    330                 335                 340

gat gta gag gga ctc cat gag aag gga agt caa gcc tca aga aag ggt   1288
Asp Val Glu Gly Leu His Glu Lys Gly Ser Gln Ala Ser Arg Lys Gly
345                 350                 355                 360

atg ctg gtt gag aag gaa agc atg gat aca att gac caa gca acc cat   1336
Met Leu Val Glu Lys Glu Ser Met Asp Thr Ile Asp Gln Ala Thr His
                365                 370                 375

ctt gtc gag caa gcc cac aac atg agg gac aaa atc caa gag atc aac   1384
Leu Val Glu Gln Ala His Asn Met Arg Asp Lys Ile Gln Glu Ile Asn
            380                 385                 390

agc aag atg ctc tac tat gga gag aat cag gaa ctt ggc ccc gag gaa   1432
Ser Lys Met Leu Tyr Tyr Gly Glu Asn Gln Glu Leu Gly Pro Glu Glu
        395                 400                 405

ata gct gag aag ctg gtg ttg gcc cag aaa atg ctg gaa gag atc cga   1480
Ile Ala Glu Lys Leu Val Leu Ala Gln Lys Met Leu Glu Glu Ile Arg
    410                 415                 420

agc cgg cag cca ttc ctc acc cat cgg gag ctg gtg gat gag gag gca   1528
Ser Arg Gln Pro Phe Leu Thr His Arg Glu Leu Val Asp Glu Glu Ala
425                 430                 435                 440

gat gag gcc cag gaa ttg ctg agc caa gct gag aac tgg cag cgg ctg   1576
Asp Glu Ala Gln Glu Leu Leu Ser Gln Ala Glu Asn Trp Gln Arg Leu
                445                 450                 455

cac aat gac acc cgc tct tta ttc ccc gtg gtg ctg gag cag ctg gac   1624
His Asn Asp Thr Arg Ser Leu Phe Pro Val Val Leu Glu Gln Leu Asp
            460                 465                 470

gac tac aac gct aag ctg tcc gac ctc cag gaa tcc att aac cag gcc   1672
Asp Tyr Asn Ala Lys Leu Ser Asp Leu Gln Glu Ser Ile Asn Gln Ala
        475                 480                 485

ctc gac cat gtc agg gat gca gaa gac atg aat aga gcc atc act ttc   1720
Leu Asp His Val Arg Asp Ala Glu Asp Met Asn Arg Ala Ile Thr Phe
    490                 495                 500

aag cag cgg gac cat gag aaa caa cat gag aga gtg aag gaa cag atg   1768
Lys Gln Arg Asp His Glu Lys Gln His Glu Arg Val Lys Glu Gln Met
505                 510                 515                 520

gaa gtt gtg ggt gcc tct ctg agt atg tct gca gac tct ctt acc ata   1816
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Glu Val Val Gly Ala Ser Leu Ser Met Ser Ala Asp Ser Leu Thr Ile
                525                 530                 535

cct cag ctc act ctt gag gaa ctt gat gag ata ata aag aat gca tct   1864
Pro Gln Leu Thr Leu Glu Glu Leu Asp Glu Ile Ile Lys Asn Ala Ser
            540                 545                 550

gga att tat gca gaa ata gat gga gcc aaa aat gag ctg caa gga aaa   1912
Gly Ile Tyr Ala Glu Ile Asp Gly Ala Lys Asn Glu Leu Gln Gly Lys
        555                 560                 565

cta tcc aac ctg agt aac ctc agt cat gac ttg gtt cag gaa gct acg   1960
Leu Ser Asn Leu Ser Asn Leu Ser His Asp Leu Val Gln Glu Ala Thr
    570                 575                 580

gac cat gca tac aat ctt caa cag gaa gcc gat gag cta agc aga aat   2008
Asp His Ala Tyr Asn Leu Gln Gln Glu Ala Asp Glu Leu Ser Arg Asn
585                 590                 595                 600

ttg cac agt tca gac atg aac ggg ctg gta cag aag gct ttg gat gca   2056
Leu His Ser Ser Asp Met Asn Gly Leu Val Gln Lys Ala Leu Asp Ala
                605                 610                 615

tca aac gtc tat gaa aat atc gcc aat tat gtc agt gaa gcc aac gaa   2104
Ser Asn Val Tyr Glu Asn Ile Ala Asn Tyr Val Ser Glu Ala Asn Glu
            620                 625                 630

aca gca gaa ctt gct ctg aat atc act gat cga att tat gat gct gtg   2152
Thr Ala Glu Leu Ala Leu Asn Ile Thr Asp Arg Ile Tyr Asp Ala Val
        635                 640                 645

agt ggg att gac acg cag atc att tac cat aag gat gaa agt gac aac   2200
Ser Gly Ile Asp Thr Gln Ile Ile Tyr His Lys Asp Glu Ser Asp Asn
    650                 655                 660

ctt ctc aat caa gcc aga gag ctg cag gcc aag gca gat tca tgc aat   2248
Leu Leu Asn Gln Ala Arg Glu Leu Gln Ala Lys Ala Asp Ser Cys Asn
665                 670                 675                 680

gat gaa gca gtg gct gac acc agc agg cgt gtg ggt gga gcc ctg tgg   2296
Asp Glu Ala Val Ala Asp Thr Ser Arg Arg Val Gly Gly Ala Leu Trp
                685                 690                 695

agg aag ggc gcc ctc aga gac aga ctg aat gat gct gtt aag caa cta   2344
Arg Lys Gly Ala Leu Arg Asp Arg Leu Asn Asp Ala Val Lys Gln Leu
            700                 705                 710

cag gca gca gag aga ggg gac gcc cac cag cgc ctg ggc cag tcc aag   2392
Gln Ala Ala Glu Arg Gly Asp Ala His Gln Arg Leu Gly Gln Ser Lys
        715                 720                 725

ctc ttc att gag gaa gct aac aag acg aca gcg gct gtc caa cag gtt   2440
Leu Phe Ile Glu Glu Ala Asn Lys Thr Thr Ala Ala Val Gln Gln Val
    730                 735                 740

acc aca cca atg gct aac aac ctc agc aac tgg tcc cag aac ctg cag   2488
Thr Thr Pro Met Ala Asn Asn Leu Ser Asn Trp Ser Gln Asn Leu Gln
745                 750                 755                 760

acc ttt gac tca tct gca tat aac act gca gtg gac tct gct cgg gac   2536
Thr Phe Asp Ser Ser Ala Tyr Asn Thr Ala Val Asp Ser Ala Arg Asp
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                765                 770                 775

gca gtg aga aac ctc acc gag gtt gtc ccc cag ctt ctg gat cag ctt   2584
Ala Val Arg Asn Leu Thr Glu Val Val Pro Gln Leu Leu Asp Gln Leu
            780                 785                 790

cgt act gtg gag cag aag cgg cct gca agc aac att tct gcc agc atc   2632
Arg Thr Val Glu Gln Lys Arg Pro Ala Ser Asn Ile Ser Ala Ser Ile
        795                 800                 805

cag agc atc cga gag ctc att gct caa acc agg agt gtc gca agc aag   2680
Gln Ser Ile Arg Glu Leu Ile Ala Gln Thr Arg Ser Val Ala Ser Lys
    810                 815                 820

atc caa gtc tcc atg atg ttt gat ggc cag tca gct gtc gaa gtg cac   2728
Ile Gln Val Ser Met Met Phe Asp Gly Gln Ser Ala Val Glu Val His
825                 830                 835                 840

ccc aaa gtc agt gtg gat gac ctg aag gcc ttc aca tcc atc agc ttg   2776
Pro Lys Val Ser Val Asp Asp Leu Lys Ala Phe Thr Ser Ile Ser Leu
                845                 850                 855

tac atg aag cct cct cca aag ccg gca gag ccc act ggg gcc tgg gta   2824
Tyr Met Lys Pro Pro Pro Lys Pro Ala Glu Pro Thr Gly Ala Trp Val
            860                 865                 870

gca gat cag ttt gtc ctc tac ctc gga agc aaa aac gcc aaa aaa gaa   2872
Ala Asp Gln Phe Val Leu Tyr Leu Gly Ser Lys Asn Ala Lys Lys Glu
        875                 880                 885

tac atg ggt ctg gca atc aaa aat gat aac ctg gta tac gtt tac aat   2920
Tyr Met Gly Leu Ala Ile Lys Asn Asp Asn Leu Val Tyr Val Tyr Asn
    890                 895                 900

ttg ggg atg aaa gat gtg gaa att ctc ctg gat tcc aag cct gtg agc   2968
Leu Gly Met Lys Asp Val Glu Ile Leu Leu Asp Ser Lys Pro Val Ser
905                 910                 915                 920

tcc tgg ccc gct tac ttt agt att gtc aag att gaa agg gta ggg gaa   3016
Ser Trp Pro Ala Tyr Phe Ser Ile Val Lys Ile Glu Arg Val Gly Glu
                925                 930                 935

cac gga aag gtg ttc ttg aca gtc ccc agt ctc agt agc aca gca gaa   3064
His Gly Lys Val Phe Leu Thr Val Pro Ser Leu Ser Ser Thr Ala Glu
            940                 945                 950

gaa aag ttt att aag aag ggg gag ttt gca gga gat gac tcc ttg ctg   3112
Glu Lys Phe Ile Lys Lys Gly Glu Phe Ala Gly Asp Asp Ser Leu Leu
        955                 960                 965

gat gtg acc cct gag gac act gtg ttt tac gtt ggt ggg gtg cct gcg   3160
Asp Val Thr Pro Glu Asp Thr Val Phe Tyr Val Gly Gly Val Pro Ala
    970                 975                 980

aac ttc aag ctc cct gcc agc tta aac ctg ccc agc tac tca ggc tgc   3208
Asn Phe Lys Leu Pro Ala Ser Leu Asn Leu Pro Ser Tyr Ser Gly Cys
985                 990                 995                1000

cta gag ctg gcc act ctg aat aat gat gtg atc agc ttg tac aac ttc   3256
Leu Glu Leu Ala Thr Leu Asn Asn Asp Val Ile Ser Leu Tyr Asn Phe
               1005                1010                1015
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Lys His Ile Tyr Asn Met Asp Pro Ser Lys Ser Val Pro Cys Ala Arg
          1020                1025                1030

gat aaa ctg gct ttc act cag agt agg gct gcc agc tac ttc ttc gat   3352
Asp Lys Leu Ala Phe Thr Gln Ser Arg Ala Ala Ser Tyr Phe Phe Asp
       1035                1040                1045

ggc tcc agt tat gca gtg gtg agg gac atc acg agg aga ggg aag ttt   3400
Gly Ser Ser Tyr Ala Val Val Arg Asp Ile Thr Arg Arg Gly Lys Phe
   1050                1055                1060

ggt cag gtg act cgc ttt gac ata gaa atc cga aca cca gct gac aat   3448
Gly Gln Val Thr Arg Phe Asp Ile Glu Ile Arg Thr Pro Ala Asp Asn
1065                1070                1075                1080

ggc ctt gtg ctc ctg atg gtc aat ggc agt atg ttt ttc agc ctc gaa   3496
Gly Leu Val Leu Leu Met Val Asn Gly Ser Met Phe Phe Ser Leu Glu
               1085                1090                1095

atg cgc aat ggc tac cta cat gtg ttc tat gac ttt gga ttc agc aat   3544
Met Arg Asn Gly Tyr Leu His Val Phe Tyr Asp Phe Gly Phe Ser Asn
          1100                1105                1110

ggc ccc gtg cat ctt gaa gac acg ttg aaa aaa gcc cag att aat gat   3592
Gly Pro Val His Leu Glu Asp Thr Leu Lys Lys Ala Gln Ile Asn Asp
       1115                1120                1125

gcg aaa tat cat gag atc tca atc att tat cac aac gac aaa aaa atg   3640
Ala Lys Tyr His Glu Ile Ser Ile Ile Tyr His Asn Asp Lys Lys Met
   1130                1135                1140

att ttg gtg gtg gac aga cgg cac gtt aag agc aca gac aat gag aag   3688
Ile Leu Val Val Asp Arg Arg His Val Lys Ser Thr Asp Asn Glu Lys
1145                1150                1155                1160

aaa aag att cct ttc acg gac atc tac atc gga ggt gcg ccc caa gaa   3736
Lys Lys Ile Pro Phe Thr Asp Ile Tyr Ile Gly Gly Ala Pro Gln Glu
               1165                1170                1175

gtc tta cag tcc agg acc cta aga gca cac ctt ccc cta gat atc aac   3784
Val Leu Gln Ser Arg Thr Leu Arg Ala His Leu Pro Leu Asp Ile Asn
          1180                1185                1190

ttt agg ggg tgc atg aag ggg ttc cag ttc caa aag aaa gat ttc aat   3832
Phe Arg Gly Cys Met Lys Gly Phe Gln Phe Gln Lys Lys Asp Phe Asn
       1195                1200                1205

tta ctg gag cag aca gaa acc cta gga gtt ggt tat gga tgc cca gag   3880
Leu Leu Glu Gln Thr Glu Thr Leu Gly Val Gly Tyr Gly Cys Pro Glu
   1210                1215                1220

gac tct ctg ata tct cgc aga gca tat ttc aat ggg caa agt ttt att   3928
Asp Ser Leu Ile Ser Arg Arg Ala Tyr Phe Asn Gly Gln Ser Phe Ile
1225                1230                1235                1240

gct tca att cag aaa ata tct ttc ttt gat ggc ttt gaa gga ggc ttc   3976
Ala Ser Ile Gln Lys Ile Ser Phe Phe Asp Gly Phe Glu Gly Gly Phe
               1245                1250                1255
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aat ttc cga aca tta cag cca aat ggg tta cta ttc tac tac aca tca   4024
Asn Phe Arg Thr Leu Gln Pro Asn Gly Leu Leu Phe Tyr Tyr Thr Ser
          1260                1265                1270

ggg tcg gac gtg ttt tcc att tca ctg gac aac ggc act gtt gtc atg   4072
Gly Ser Asp Val Phe Ser Ile Ser Leu Asp Asn Gly Thr Val Val Met
      1275                1280                1285

gac gta aag ggc atc aag gtc atg tca aca gac aag cag tac cac gat   4120
Asp Val Lys Gly Ile Lys Val Met Ser Thr Asp Lys Gln Tyr His Asp
   1290                1295                1300

ggg ctg ccc cac ttc gtg gtc acc tcc atc tca gac aca aga tat gaa   4168
Gly Leu Pro His Phe Val Val Thr Ser Ile Ser Asp Thr Arg Tyr Glu
1305                1310                1315                1320

ctg gta gta gac aaa agc cga ctt cga ggg aag aat cca aca aaa ggg   4216
Leu Val Val Asp Lys Ser Arg Leu Arg Gly Lys Asn Pro Thr Lys Gly
               1325                1330                1335

aag gca gag cag act caa aca act gag aag aag ttc tac ttt ggt ggc   4264
Lys Ala Glu Gln Thr Gln Thr Thr Glu Lys Lys Phe Tyr Phe Gly Gly
          1340                1345                1350

tca ccc atc agt cct cag tat gct aat ttc act gga tgt ata agc aat   4312
Ser Pro Ile Ser Pro Gln Tyr Ala Asn Phe Thr Gly Cys Ile Ser Asn
      1355                1360                1365

gcc tac ttt acc agg ttg gat aga gat gtg gaa gtc gaa gac ttc cag   4360
Ala Tyr Phe Thr Arg Leu Asp Arg Asp Val Glu Val Glu Asp Phe Gln
   1370                1375                1380

cgc tat tct gaa aag gtc cac act tca ctc tat gag tgt ccg att gag   4408
Arg Tyr Ser Glu Lys Val His Thr Ser Leu Tyr Glu Cys Pro Ile Glu
1385                1390                1395                1400

tcg tca cct ctg ttt ctc ctt cac aaa aaa gga aag aat tcc tca aag   4456
Ser Ser Pro Leu Phe Leu Leu His Lys Lys Gly Lys Asn Ser Ser Lys
               1405                1410                1415

cct aaa aca aac aaa cag gga gag aag agt aag gat gcg cct tca tgg   4504
Pro Lys Thr Asn Lys Gln Gly Glu Lys Ser Lys Asp Ala Pro Ser Trp
          1420                1425                1430

gat cct att ggc ctg aag ttt ctg gaa cag aaa gct cca aga gat tcc   4552
Asp Pro Ile Gly Leu Lys Phe Leu Glu Gln Lys Ala Pro Arg Asp Ser
      1435                1440                1445

cac tgc cac ctc tcc agc agc ccc agg gca ata gaa cat gcc tat caa   4600
His Cys His Leu Ser Ser Ser Pro Arg Ala Ile Glu His Ala Tyr Gln
   1450                1455                1460

tat ggc ggc acg gcc aac agt cgc cag gag ttt gaa cac gaa caa gga   4648
Tyr Gly Gly Thr Ala Asn Ser Arg Gln Glu Phe Glu His Glu Gln Gly
1465                1470                1475                1480

gat ttt ggt gaa aaa tcc cag ttt gcc att cgt ctg aag acc cgt tcc   4696
Asp Phe Gly Glu Lys Ser Gln Phe Ala Ile Arg Leu Lys Thr Arg Ser
               1485                1490                1495

tca cat ggg atg att ttc tat gtc tca gac caa gaa gag aat gat ttc   4744
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Ser His Gly Met Ile Phe Tyr Val Ser Asp Gln Glu Glu Asn Asp Phe
          1500                1505                1510

atg acc ctg ttc ttg gcc cat ggt cgc ttg gtc ttt atg ttt aat gtt   4792
Met Thr Leu Phe Leu Ala His Gly Arg Leu Val Phe Met Phe Asn Val
       1515                1520                1525

ggc cat aag aaa ctg aag att aga agc cag gag aaa tac aat gat gga   4840
Gly His Lys Lys Leu Lys Ile Arg Ser Gln Glu Lys Tyr Asn Asp Gly
   1530                1535                1540

ttg tgg cat gat gtg ata ttt att cgg gaa aag agc agt ggt cga ctg   4888
Leu Trp His Asp Val Ile Phe Ile Arg Glu Lys Ser Ser Gly Arg Leu
1545                1550                1555                1560

gtc att gat ggt cta cga gtc cta gaa gaa agg ctt ccc cct agt ggc   4936
Val Ile Asp Gly Leu Arg Val Leu Glu Glu Arg Leu Pro Pro Ser Gly
               1565                1570                1575

gct gcc tgg aaa atc aag ggt ccc att tat ctg gga gga gtg gct ccc   4984
Ala Ala Trp Lys Ile Lys Gly Pro Ile Tyr Leu Gly Gly Val Ala Pro
          1580                1585                1590

gga aga gcc gtg aaa aat gtc cag att acc tcc gtc tac agc ttc agt   5032
Gly Arg Ala Val Lys Asn Val Gln Ile Thr Ser Val Tyr Ser Phe Ser
       1595                1600                1605

ggc tgc ctt ggc aat ctc cag ctc aat ggt gcc tcc atc acc tcc gct   5080
Gly Cys Leu Gly Asn Leu Gln Leu Asn Gly Ala Ser Ile Thr Ser Ala
   1610                1615                1620

tct caa acg ttt agc gtg acc cct tgc ttt gaa ggg cca atg gaa aca   5128
Ser Gln Thr Phe Ser Val Thr Pro Cys Phe Glu Gly Pro Met Glu Thr
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gga act tat ttt tcc aca gaa ggc ggc tat gtg gtt cta gat gag tct   5176
Gly Thr Tyr Phe Ser Thr Glu Gly Gly Tyr Val Val Leu Asp Glu Ser
               1645                1650                1655

ttc aat att ggg tta aaa ttt gaa att gcc ttt gaa gtc cgc ccc cgg   5224
Phe Asn Ile Gly Leu Lys Phe Glu Ile Ala Phe Glu Val Arg Pro Arg
          1660                1665                1670

agc agt tct gga acc ctt gtc cat ggc cac agc gtc aac ggg gaa tac   5272
Ser Ser Ser Gly Thr Leu Val His Gly His Ser Val Asn Gly Glu Tyr
       1675                1680                1685

ctg aac gtg cac atg aga aac gga cag gtc ata gtg aag gtc aac aac   5320
Leu Asn Val His Met Arg Asn Gly Gln Val Ile Val Lys Val Asn Asn
   1690                1695                1700

ggt gtc aga gac ttt tct acc tca gta act ccc aag cag aat ctc tgt   5368
Gly Val Arg Asp Phe Ser Thr Ser Val Thr Pro Lys Gln Asn Leu Cys
1705                1710                1715                1720

gat ggc aga tgg cac aga att aca gtt att aga gat tca aac gtg gtt   5416
Asp Gly Arg Trp His Arg Ile Thr Val Ile Arg Asp Ser Asn Val Val
               1725                1730                1735

cag ttg gat gta gac tca gaa gtg aac cat gta gtt ggg ccg ttg aat   5464
Gln Leu Asp Val Asp Ser Glu Val Asn His Val Val Gly Pro Leu Asn
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          1740                1745                1750

cca aag cca gtt gat cac agg gag cct gtg ttt gtt gga ggt gtt cca   5512
Pro Lys Pro Val Asp His Arg Glu Pro Val Phe Val Gly Gly Val Pro
       1755                1760                1765

gag tct tta ctg aca cca cgt ttg gct ccc agc aaa ccc ttc acc ggc   5560
Glu Ser Leu Leu Thr Pro Arg Leu Ala Pro Ser Lys Pro Phe Thr Gly
   1770                1775                1780

tgc atc cgc cac ttt gta att gac agc cgc cct gtg agc ttc agt aaa   5608
Cys Ile Arg His Phe Val Ile Asp Ser Arg Pro Val Ser Phe Ser Lys
1785                1790                1795                1800

gct gcc ctg gtc agt ggt gct gtg agc atc aac tcc tgt ccc aca gcc   5656
Ala Ala Leu Val Ser Gly Ala Val Ser Ile Asn Ser Cys Pro Thr Ala
               1805                1810                1815

tgacacagct gcaaggctgc tgaagacagc tcttcctaac actgaaataa acatagtagt 5716

gggggtcgg gagggtcaga ggcctggaac tcccctccct actgaagctc tcacctggtt 5776

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Pro Phe Asp Ile Glu Gly Ser Ala Val Val Gly Arg Gln Asp Pro Ser
         35                  40                  45

Glu Thr Ser Asp Ser Gly Val Thr Leu Gly Arg Leu Pro Pro Ala Ala
     50                  55                  60

Glu Arg Cys Asp Ala Gly Phe Phe Arg Thr Leu Ser Gly Glu Cys Ala
 65                  70                  75                  80

Pro Cys Asp Cys Asn Gly Asn Ser His Glu Cys Leu Asp Gly Ser Gly
                 85                  90                  95

Phe Cys Leu His Cys Gln Arg Asn Thr Thr Gly Glu His Cys Glu Lys
            100                 105                 110

Cys Leu Asp Gly Tyr Ile Gly Asp Ser Ile Arg Gly Thr Pro Arg Phe
        115                 120                 125

Cys Gln Pro Cys Pro Cys Pro Leu Pro His Leu Ala Asn Phe Ala Glu
    130                 135                 140

Ser Cys Tyr Arg Lys Asn Gly Ala Val Arg Cys Ile Cys Lys Glu Asn
145                 150                 155                 160
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Tyr Val Gly Pro Asn Cys Glu Arg Cys Ala Pro Gly Tyr Tyr Gly Asn
                165                 170                 175

Pro Leu Leu Ile Gly Ser Thr Cys Lys Lys Cys Asp Cys Ser Gly Asn
            180                 185                 190

Ser Asp Pro Asn Leu Ile Phe Glu Asp Cys Asp Glu Ile Thr Gly Gln
        195                 200                 205

Cys Arg Asn Cys Leu Arg Asn Thr Thr Gly Phe Lys Cys Glu Arg Cys
    210                 215                 220

Ala Pro Gly Tyr Tyr Gly Asp Ala Arg Thr Ala Lys Asn Cys Ala Val
225                 230                 235                 240

Cys Asn Cys Gly Gly Gly Pro Arg Asp Ser Val Thr Gly Glu Cys Leu
                245                 250                 255

Glu Glu Gly Phe Glu Val Pro Thr Gly Cys Asp Lys Cys Val Trp Asp
            260                 265                 270

Leu Thr Asp Asp Leu Arg Leu Ala Ala Leu Ser Ile Glu Glu Ser Lys
        275                 280                 285

Ser Gly Leu Leu Ser Val Ser Ser Ala Ala Ala Ala His Arg His Val
    290                 295                 300

Thr Asp Met Asn Ser Thr Ile His Leu Leu Arg Thr Arg Leu Ser Glu
305                 310                 315                 320

Arg Glu Asn Gln Tyr Thr Leu Arg Lys Ile Gln Ile Asn Asn Ser Glu
                325                 330                 335

Asn Thr Leu Arg Ser Leu Leu Pro Asp Val Glu Gly Leu His Glu Lys
            340                 345                 350

Gly Ser Gln Ala Ser Arg Lys Gly Met Leu Val Glu Lys Glu Ser Met
        355                 360                 365

Asp Thr Ile Asp Gln Ala Thr His Leu Val Glu Gln Ala His Asn Met
    370                 375                 380

Arg Asp Lys Ile Gln Glu Ile Asn Ser Lys Met Leu Tyr Tyr Gly Glu
385                 390                 395                 400

Asn Gln Glu Leu Gly Pro Glu Glu Ile Ala Glu Lys Leu Val Leu Ala
                405                 410                 415

Gln Lys Met Leu Glu Glu Ile Arg Ser Arg Gln Pro Phe Leu Thr His
            420                 425                 430

Arg Glu Leu Val Asp Glu Glu Ala Asp Glu Ala Gln Glu Leu Leu Ser
        435                 440                 445

Gln Ala Glu Asn Trp Gln Arg Leu His Asn Asp Thr Arg Ser Leu Phe
    450                 455                 460

Pro Val Val Leu Glu Gln Leu Asp Asp Tyr Asn Ala Lys Leu Ser Asp
465                 470                 475                 480

Leu Gln Glu Ser Ile Asn Gln Ala Leu Asp His Val Arg Asp Ala Glu
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485 490 495

Asp Met Asn Arg Ala Ile Thr Phe Lys Gln Arg Asp His Glu Lys Gln
500 505 510

His Glu Arg Val Lys Glu Gln Met Glu Val Val Gly Ala Ser Leu Ser
515 520 525

Met Ser Ala Asp Ser Leu Thr Ile Pro Gln Leu Thr Leu Glu Glu Leu
530 535 540

Asp Glu Ile Ile Lys Asn Ala Ser Gly Ile Tyr Ala Glu Ile Asp Gly
545 550 555 560

Ala Lys Asn Glu Leu Gln Gly Lys Leu Ser Asn Leu Ser Asn Leu Ser
565 570 575

His Asp Leu Val Gln Glu Ala Thr Asp His Ala Tyr Asn Leu Gln Gln
580 585 590

Glu Ala Asp Glu Leu Ser Arg Asn Leu His Ser Ser Asp Met Asn Gly
595 600 605

Leu Val Gln Lys Ala Leu Asp Ala Ser Asn Val Tyr Glu Asn Ile Ala
610 615 620

Asn Tyr Val Ser Glu Ala Asn Glu Thr Ala Glu Leu Ala Leu Asn Ile
625 630 635 640

Thr Asp Arg Ile Tyr Asp Ala Val Ser Gly Ile Asp Thr Gln Ile Ile
645 650 655

Tyr His Lys Asp Glu Ser Asp Asn Leu Leu Asn Gln Ala Arg Glu Leu
660 665 670

Gln Ala Lys Ala Asp Ser Cys Asn Asp Glu Ala Val Ala Asp Thr Ser
675 680 685

Arg Arg Val Gly Gly Ala Leu Trp Arg Lys Gly Ala Leu Arg Asp Arg
690 695 700

Leu Asn Asp Ala Val Lys Gln Leu Gln Ala Ala Glu Arg Gly Asp Ala
705 710 715 720

His Gln Arg Leu Gly Gln Ser Lys Leu Phe Ile Glu Glu Ala Asn Lys
725 730 735

Thr Thr Ala Ala Val Gln Gln Val Thr Thr Pro Met Ala Asn Asn Leu
740 745 750

Ser Asn Trp Ser Gln Asn Leu Gln Thr Phe Asp Ser Ser Ala Tyr Asn
755 760 765

Thr Ala Val Asp Ser Ala Arg Asp Ala Val Arg Asn Leu Thr Glu Val
770 775 780

Val Pro Gln Leu Leu Asp Gln Leu Arg Thr Val Glu Gln Lys Arg Pro
785 790 795 800

Ala Ser Asn Ile Ser Ala Ser Ile Gln Ser Ile Arg Glu Leu Ile Ala
805 810 815

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Gln Thr Arg Ser Val Ala Ser Lys Ile Gln Val Ser Met Met Phe Asp
            820                 825                 830

Gly Gln Ser Ala Val Glu Val His Pro Lys Val Ser Val Asp Asp Leu
        835                 840                 845

Lys Ala Phe Thr Ser Ile Ser Leu Tyr Met Lys Pro Pro Pro Lys Pro
    850                 855                 860

Ala Glu Pro Thr Gly Ala Trp Val Ala Asp Gln Phe Val Leu Tyr Leu
865                 870                 875                 880

Gly Ser Lys Asn Ala Lys Lys Glu Tyr Met Gly Leu Ala Ile Lys Asn
                885                 890                 895

Asp Asn Leu Val Tyr Val Tyr Asn Leu Gly Met Lys Asp Val Glu Ile
            900                 905                 910

Leu Leu Asp Ser Lys Pro Val Ser Ser Trp Pro Ala Tyr Phe Ser Ile
        915                 920                 925

Val Lys Ile Glu Arg Val Gly Glu His Gly Lys Val Phe Leu Thr Val
    930                 935                 940

Pro Ser Leu Ser Ser Thr Ala Glu Glu Lys Phe Ile Lys Lys Gly Glu
945                 950                 955                 960

Phe Ala Gly Asp Asp Ser Leu Leu Asp Val Thr Pro Glu Asp Thr Val
                965                 970                 975

Phe Tyr Val Gly Gly Val Pro Ala Asn Phe Lys Leu Pro Ala Ser Leu
            980                 985                 990

Asn Leu Pro Ser Tyr Ser Gly Cys Leu Glu Leu Ala Thr Leu Asn Asn
        995                1000                1005

Asp Val Ile Ser Leu Tyr Asn Phe Lys His Ile Tyr Asn Met Asp Pro
   1010                1015                1020

Ser Lys Ser Val Pro Cys Ala Arg Asp Lys Leu Ala Phe Thr Gln Ser
025                1030                1035                1040

Arg Ala Ala Ser Tyr Phe Phe Asp Gly Ser Ser Tyr Ala Val Val Arg
               1045                1050                1055

Asp Ile Thr Arg Arg Gly Lys Phe Gly Gln Val Thr Arg Phe Asp Ile
           1060                1065                1070

Glu Ile Arg Thr Pro Ala Asp Asn Gly Leu Val Leu Leu Met Val Asn
       1075                1080                1085

Gly Ser Met Phe Phe Ser Leu Glu Met Arg Asn Gly Tyr Leu His Val
   1090                1095                1100

Phe Tyr Asp Phe Gly Phe Ser Asn Gly Pro Val His Leu Glu Asp Thr
105                1110                1115                1120

Leu Lys Lys Ala Gln Ile Asn Asp Ala Lys Tyr His Glu Ile Ser Ile
               1125                1130                1135
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Ile Tyr His Asn Asp Lys Lys Met Ile Leu Val Val Asp Arg Arg His
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Val Lys Ser Thr Asp Asn Glu Lys Lys Lys Ile Pro Phe Thr Asp Ile
1155 1160 1165

Tyr Ile Gly Gly Ala Pro Gln Glu Val Leu Gln Ser Arg Thr Leu Arg
1170 1175 1180

Ala His Leu Pro Leu Asp Ile Asn Phe Arg Gly Cys Met Lys Gly Phe
185 1190 1195 1200

Gln Phe Gln Lys Lys Asp Phe Asn Leu Leu Glu Gln Thr Glu Thr Leu
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Gly Val Gly Tyr Gly Cys Pro Glu Asp Ser Leu Ile Ser Arg Arg Ala
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Tyr Phe Asn Gly Gln Ser Phe Ile Ala Ser Ile Gln Lys Ile Ser Phe
1235 1240 1245

Phe Asp Gly Phe Glu Gly Gly Phe Asn Phe Arg Thr Leu Gln Pro Asn
1250 1255 1260

Gly Leu Leu Phe Tyr Tyr Thr Ser Gly Ser Asp Val Phe Ser Ile Ser
265 1270 1275 1280

Leu Asp Asn Gly Thr Val Val Met Asp Val Lys Gly Ile Lys Val Met
1285 1290 1295

Ser Thr Asp Lys Gln Tyr His Asp Gly Leu Pro His Phe Val Val Thr
1300 1305 1310

Ser Ile Ser Asp Thr Arg Tyr Glu Leu Val Val Asp Lys Ser Arg Leu
1315 1320 1325

Arg Gly Lys Asn Pro Thr Lys Gly Lys Ala Glu Gln Thr Gln Thr Thr
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Glu Lys Lys Phe Tyr Phe Gly Gly Ser Pro Ile Ser Pro Gln Tyr Ala
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Asn Phe Thr Gly Cys Ile Ser Asn Ala Tyr Phe Thr Arg Leu Asp Arg
1365 1370 1375

Asp Val Glu Val Glu Asp Phe Gln Arg Tyr Ser Glu Lys Val His Thr
1380 1385 1390

Ser Leu Tyr Glu Cys Pro Ile Glu Ser Ser Pro Leu Phe Leu Leu His
1395 1400 1405

Lys Lys Gly Lys Asn Ser Ser Lys Pro Lys Thr Asn Lys Gln Gly Glu
1410 1415 1420

Lys Ser Lys Asp Ala Pro Ser Trp Asp Pro Ile Gly Leu Lys Phe Leu
425 1430 1435 1440

Glu Gln Lys Ala Pro Arg Asp Ser His Cys His Leu Ser Ser Ser Pro
1445 1450 1455

Arg Ala Ile Glu His Ala Tyr Gln Tyr Gly Gly Thr Ala Asn Ser Arg

1460 1465 1470

Gln Glu Phe Glu His Glu Gln Gly Asp Phe Gly Glu Lys Ser Gln Phe
1475 1480 1485

Ala Ile Arg Leu Lys Thr Arg Ser Ser His Gly Met Ile Phe Tyr Val
1490 1495 1500

Ser Asp Gln Glu Glu Asn Asp Phe Met Thr Leu Phe Leu Ala His Gly
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Arg Leu Val Phe Met Phe Asn Val Gly His Lys Lys Leu Lys Ile Arg
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Ser Gln Glu Lys Tyr Asn Asp Gly Leu Trp His Asp Val Ile Phe Ile
1540 1545 1550

Arg Glu Lys Ser Ser Gly Arg Leu Val Ile Asp Gly Leu Arg Val Leu
1555 1560 1565

Glu Glu Arg Leu Pro Pro Ser Gly Ala Ala Trp Lys Ile Lys Gly Pro
1570 1575 1580

Ile Tyr Leu Gly Gly Val Ala Pro Gly Arg Ala Val Lys Asn Val Gln
585 1590 1595 1600

Ile Thr Ser Val Tyr Ser Phe Ser Gly Cys Leu Gly Asn Leu Gln Leu
1605 1610 1615

Asn Gly Ala Ser Ile Thr Ser Ala Ser Gln Thr Phe Ser Val Thr Pro
1620 1625 1630

Cys Phe Glu Gly Pro Met Glu Thr Gly Thr Tyr Phe Ser Thr Glu Gly
1635 1640 1645

Gly Tyr Val Val Leu Asp Glu Ser Phe Asn Ile Gly Leu Lys Phe Glu
1650 1655 1660

Ile Ala Phe Glu Val Arg Pro Arg Ser Ser Ser Gly Thr Leu Val His
665 1670 1675 1680

Gly His Ser Val Asn Gly Glu Tyr Leu Asn Val His Met Arg Asn Gly
1685 1690 1695

Gln Val Ile Val Lys Val Asn Asn Gly Val Arg Asp Phe Ser Thr Ser
1700 1705 1710

Val Thr Pro Lys Gln Asn Leu Cys Asp Gly Arg Trp His Arg Ile Thr
1715 1720 1725

Val Ile Arg Asp Ser Asn Val Val Gln Leu Asp Val Asp Ser Glu Val
1730 1735 1740

Asn His Val Val Gly Pro Leu Asn Pro Lys Pro Val Asp His Arg Glu
745 1750 1755 1760

Pro Val Phe Val Gly Gly Val Pro Glu Ser Leu Leu Thr Pro Arg Leu
1765 1770 1775

Ala Pro Ser Lys Pro Phe Thr Gly Cys Ile Arg His Phe Val Ile Asp
1780 1785 1790

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Ser Ile Asn Ser Cys Pro Thr Ala
   1810                1815


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gtg gtc ggc agg caa gac cca tcg gag act agc gac tca ggc gtg aca   96
Val Val Gly Arg Gln Asp Pro Ser Glu Thr Ser Asp Ser Gly Val Thr
             20                  25                  30

ctg gga cgc ctg ccg cct gct gct gag aga tgt gac gct gga ttc ttc   144
Leu Gly Arg Leu Pro Pro Ala Ala Glu Arg Cys Asp Ala Gly Phe Phe
         35                  40                  45

cgc aca ctg tca gga gaa tgt gca ccc tgt gac tgt aat ggc aat tcc   192
Arg Thr Leu Ser Gly Glu Cys Ala Pro Cys Asp Cys Asn Gly Asn Ser
     50                  55                  60

cat gag tgc ttg gat ggc tcc gga ttc tgt ctg cac tgc cag cgg aac   240
His Glu Cys Leu Asp Gly Ser Gly Phe Cys Leu His Cys Gln Arg Asn
 65                  70                  75                  80

aca aca gga gag cac tgt gaa aaa tgt ctg gat ggc tat att gga gac   288
Thr Thr Gly Glu His Cys Glu Lys Cys Leu Asp Gly Tyr Ile Gly Asp
                 85                  90                  95

tcc atc aga ggc aca ccc cgg ttc tgc cag ccg tgc ccc tgt ccc ttg   336
Ser Ile Arg Gly Thr Pro Arg Phe Cys Gln Pro Cys Pro Cys Pro Leu
            100                 105                 110

ccc cac ctg gcc aac ttt gca gaa tcc tgc tac agg aaa aat gga gct   384
Pro His Leu Ala Asn Phe Ala Glu Ser Cys Tyr Arg Lys Asn Gly Ala
        115                 120                 125

gtt cgg tgt att tgt aaa gaa aac tat gtt gga cct aac tgt gaa aga   432
Val Arg Cys Ile Cys Lys Glu Asn Tyr Val Gly Pro Asn Cys Glu Arg
    130                 135                 140

tgt gct cct ggt tac tat gga aac ccc tta ctc att gga agc acc tgt   480
Cys Ala Pro Gly Tyr Tyr Gly Asn Pro Leu Leu Ile Gly Ser Thr Cys
145                 150                 155                 160

aag aaa tgt gac tgc agt gga aat tcg gat ccc aac ctg atc ttt gaa   528
Lys Lys Cys Asp Cys Ser Gly Asn Ser Asp Pro Asn Leu Ile Phe Glu
                165                 170                 175
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gat gag gcc cag gaa ttg ctg agc caa gct gag aac tgg cag cgg ctg   1296
Asp Glu Ala Gln Glu Leu Leu Ser Gln Ala Glu Asn Trp Gln Arg Leu
            420                 425                 430

cac aat gac acc cgc tct tta ttc ccc gtg gtg ctg gag cag ctg gac   1344
His Asn Asp Thr Arg Ser Leu Phe Pro Val Val Leu Glu Gln Leu Asp
        435                 440                 445

gac tac aac gct aag ctg tcc gac ctc cag gaa tcc att aac cag gcc   1392
Asp Tyr Asn Ala Lys Leu Ser Asp Leu Gln Glu Ser Ile Asn Gln Ala
    450                 455                 460

ctc gac cat gtc agg gat gca gaa gac atg aat aga gcc atc act ttc   1440
Leu Asp His Val Arg Asp Ala Glu Asp Met Asn Arg Ala Ile Thr Phe
465                 470                 475                 480

aag cag cgg gac cat gag aaa caa cat gag aga gtg aag gaa cag atg   1488
Lys Gln Arg Asp His Glu Lys Gln His Glu Arg Val Lys Glu Gln Met
                485                 490                 495

gaa gtt gtg ggt gcc tct ctg agt atg tct gca gac tct ctt acc ata   1536
Glu Val Val Gly Ala Ser Leu Ser Met Ser Ala Asp Ser Leu Thr Ile
            500                 505                 510

cct cag ctc act ctt gag gaa ctt gat gag ata ata aag aat gca tct   1584
Pro Gln Leu Thr Leu Glu Glu Leu Asp Glu Ile Ile Lys Asn Ala Ser
        515                 520                 525

gga att tat gca gaa ata gat gga gcc aaa aat gag ctg caa gga aaa   1632
Gly Ile Tyr Ala Glu Ile Asp Gly Ala Lys Asn Glu Leu Gln Gly Lys
    530                 535                 540

cta tcc aac ctg agt aac ctc agt cat gac ttg gtt cag gaa gct acg   1680
Leu Ser Asn Leu Ser Asn Leu Ser His Asp Leu Val Gln Glu Ala Thr
545                 550                 555                 560

gac cat gca tac aat ctt caa cag gaa gcc gat gag cta agc aga aat   1728
Asp His Ala Tyr Asn Leu Gln Gln Glu Ala Asp Glu Leu Ser Arg Asn
                565                 570                 575

ttg cac agt tca gac atg aac ggg ctg gta cag aag gct ttg gat gca   1776
Leu His Ser Ser Asp Met Asn Gly Leu Val Gln Lys Ala Leu Asp Ala
            580                 585                 590

tca aac gtc tat gaa aat atc gcc aat tat gtc agt gaa gcc aac gaa   1824
Ser Asn Val Tyr Glu Asn Ile Ala Asn Tyr Val Ser Glu Ala Asn Glu
        595                 600                 605

aca gca gaa ctt gct ctg aat atc act gat cga att tat gat gct gtg   1872
Thr Ala Glu Leu Ala Leu Asn Ile Thr Asp Arg Ile Tyr Asp Ala Val
    610                 615                 620

agt ggg att gac acg cag atc att tac cat aag gat gaa agt gac aac   1920
Ser Gly Ile Asp Thr Gln Ile Ile Tyr His Lys Asp Glu Ser Asp Asn
625                 630                 635                 640

ctt ctc aat caa gcc aga gag ctg cag gcc aag gca gat tca tgc aat   1968
Leu Leu Asn Gln Ala Arg Glu Leu Gln Ala Lys Ala Asp Ser Cys Asn
                645                 650                 655

gat gaa gca gtg gct gac acc agc agg cgt gtg ggt gga gcc ctg tgg   2016
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Asp Glu Ala Val Ala Asp Thr Ser Arg Arg Val Gly Gly Ala Leu Trp
            660                 665                 670

agg aag ggc gcc ctc aga gac aga ctg aat gat gct gtt aag caa cta   2064
Arg Lys Gly Ala Leu Arg Asp Arg Leu Asn Asp Ala Val Lys Gln Leu
        675                 680                 685

cag gca gca gag aga ggg gac gcc cac cag cgc ctg ggc cag tcc aag   2112
Gln Ala Ala Glu Arg Gly Asp Ala His Gln Arg Leu Gly Gln Ser Lys
    690                 695                 700

ctc ttc att gag gaa gct aac aag acg aca gcg gct gtc caa cag gtt   2160
Leu Phe Ile Glu Glu Ala Asn Lys Thr Thr Ala Ala Val Gln Gln Val
705                 710                 715                 720

acc aca cca atg gct aac aac ctc agc aac tgg tcc cag aac ctg cag   2208
Thr Thr Pro Met Ala Asn Asn Leu Ser Asn Trp Ser Gln Asn Leu Gln
                725                 730                 735

acc ttt gac tca tct gca tat aac act gca gtg gac tct gct cgg gac   2256
Thr Phe Asp Ser Ser Ala Tyr Asn Thr Ala Val Asp Ser Ala Arg Asp
            740                 745                 750

gca gtg aga aac ctc acc gag gtt gtc ccc cag ctt ctg gat cag ctt   2304
Ala Val Arg Asn Leu Thr Glu Val Val Pro Gln Leu Leu Asp Gln Leu
        755                 760                 765

cgt act gtg gag cag aag cgg cct gca agc aac att tct gcc agc atc   2352
Arg Thr Val Glu Gln Lys Arg Pro Ala Ser Asn Ile Ser Ala Ser Ile
    770                 775                 780

cag agc atc cga gag ctc att gct caa acc agg agt gtc gca agc aag   2400
Gln Ser Ile Arg Glu Leu Ile Ala Gln Thr Arg Ser Val Ala Ser Lys
785                 790                 795                 800

atc caa gtc tcc atg atg ttt gat ggc cag tca gct gtc gaa gtg cac   2448
Ile Gln Val Ser Met Met Phe Asp Gly Gln Ser Ala Val Glu Val His
                805                 810                 815

ccc aaa gtc agt gtg gat gac ctg aag gcc ttc aca tcc atc agc ttg   2496
Pro Lys Val Ser Val Asp Asp Leu Lys Ala Phe Thr Ser Ile Ser Leu
            820                 825                 830

tac atg aag cct cct cca aag ccg gca gag ccc act ggg gcc tgg gta   2544
Tyr Met Lys Pro Pro Pro Lys Pro Ala Glu Pro Thr Gly Ala Trp Val
        835                 840                 845

gca gat cag ttt gtc ctc tac ctc gga agc aaa aac gcc aaa aaa gaa   2592
Ala Asp Gln Phe Val Leu Tyr Leu Gly Ser Lys Asn Ala Lys Lys Glu
    850                 855                 860

tac atg ggt ctg gca atc aaa aat gat aac ctg gta tac gtt tac aat   2640
Tyr Met Gly Leu Ala Ile Lys Asn Asp Asn Leu Val Tyr Val Tyr Asn
865                 870                 875                 880

ttg ggg atg aaa gat gtg gaa att ctc ctg gat tcc aag cct gtg agc   2688
Leu Gly Met Lys Asp Val Glu Ile Leu Leu Asp Ser Lys Pro Val Ser
                885                 890                 895

tcc tgg ccc gct tac ttt agt att gtc aag att gaa agg gta ggg gaa   2736
Ser Trp Pro Ala Tyr Phe Ser Ile Val Lys Ile Glu Arg Val Gly Glu
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            900                 905                 910

cac gga aag gtg ttc ttg aca gtc ccc agt ctc agt agc aca gca gaa   2784
His Gly Lys Val Phe Leu Thr Val Pro Ser Leu Ser Ser Thr Ala Glu
        915                 920                 925

gaa aag ttt att aag aag ggg gag ttt gca gga gat gac tcc ttg ctg   2832
Glu Lys Phe Ile Lys Lys Gly Glu Phe Ala Gly Asp Asp Ser Leu Leu
    930                 935                 940

gat gtg acc cct gag gac act gtg ttt tac gtt ggt ggg gtg cct gcg   2880
Asp Val Thr Pro Glu Asp Thr Val Phe Tyr Val Gly Gly Val Pro Ala
945                 950                 955                 960

aac ttc aag ctc cct gcc agc tta aac ctg ccc agc tac tca ggc tgc   2928
Asn Phe Lys Leu Pro Ala Ser Leu Asn Leu Pro Ser Tyr Ser Gly Cys
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cta gag ctg gcc act ctg aat aat gat gtg atc agc ttg tac aac ttc   2976
Leu Glu Leu Ala Thr Leu Asn Asn Asp Val Ile Ser Leu Tyr Asn Phe
            980                 985                 990

aag cac atc tat aat atg gat cca tca aag tca gtg ccc tgt gcc agg   3024
Lys His Ile Tyr Asn Met Asp Pro Ser Lys Ser Val Pro Cys Ala Arg
        995                1000                1005

gat aaa ctg gct ttc act cag agt agg gct gcc agc tac ttc ttc gat   3072
Asp Lys Leu Ala Phe Thr Gln Ser Arg Ala Ala Ser Tyr Phe Phe Asp
   1010                1015                1020

ggc tcc agt tat gca gtg gtg agg gac atc acg agg aga ggg aag ttt   3120
Gly Ser Ser Tyr Ala Val Val Arg Asp Ile Thr Arg Arg Gly Lys Phe
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ggt cag gtg act cgc ttt gac ata gaa atc cga aca cca gct gac aat   3168
Gly Gln Val Thr Arg Phe Asp Ile Glu Ile Arg Thr Pro Ala Asp Asn
                1045                1050                1055

ggc ctt gtg ctc ctg atg gtc aat ggc agt atg ttt ttc agc ctc gaa   3216
Gly Leu Val Leu Leu Met Val Asn Gly Ser Met Phe Phe Ser Leu Glu
            1060                1065                1070

atg cgc aat ggc tac cta cat gtg ttc tat gac ttt gga ttc agc aat   3264
Met Arg Asn Gly Tyr Leu His Val Phe Tyr Asp Phe Gly Phe Ser Asn
        1075                1080                1085

ggc ccc gtg cat ctt gaa gac acg ttg aaa aaa gcc cag att aat gat   3312
Gly Pro Val His Leu Glu Asp Thr Leu Lys Lys Ala Gln Ile Asn Asp
   1090                1095                1100

gcg aaa tat cat gag atc tca atc att tat cac aac gac aaa aaa atg   3360
Ala Lys Tyr His Glu Ile Ser Ile Ile Tyr His Asn Asp Lys Lys Met
1105                1110                1115                1120

att ttg gtg gtg gac aga cgg cac gtt aag agc aca gac aat gag aag   3408
Ile Leu Val Val Asp Arg Arg His Val Lys Ser Thr Asp Asn Glu Lys
                1125                1130                1135

aaa aag att cct ttc acg gac atc tac atc gga ggt gcg ccc caa gaa   3456
Lys Lys Ile Pro Phe Thr Asp Ile Tyr Ile Gly Gly Ala Pro Gln Glu
            1140                1145                1150
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gtc tta cag tcc agg acc cta aga gca cac ctt ccc cta gat atc aac   3504
Val Leu Gln Ser Arg Thr Leu Arg Ala His Leu Pro Leu Asp Ile Asn
       1155                1160                1165

ttt agg ggg tgc atg aag ggg ttc cag ttc caa aag aaa gat ttc aat   3552
Phe Arg Gly Cys Met Lys Gly Phe Gln Phe Gln Lys Lys Asp Phe Asn
   1170                1175                1180

tta ctg gag cag aca gaa acc cta gga gtt ggt tat gga tgc cca gag   3600
Leu Leu Glu Gln Thr Glu Thr Leu Gly Val Gly Tyr Gly Cys Pro Glu
1185                1190                1195                1200

gac tct ctg ata tct cgc aga gca tat ttc aat ggg caa agt ttt att   3648
Asp Ser Leu Ile Ser Arg Arg Ala Tyr Phe Asn Gly Gln Ser Phe Ile
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gct tca att cag aaa ata tct ttc ttt gat ggc ttt gaa gga ggc ttc   3696
Ala Ser Ile Gln Lys Ile Ser Phe Phe Asp Gly Phe Glu Gly Gly Phe
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aat ttc cga aca tta cag cca aat ggg tta cta ttc tac tac aca tca   3744
Asn Phe Arg Thr Leu Gln Pro Asn Gly Leu Leu Phe Tyr Tyr Thr Ser
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ggg tcg gac gtg ttt tcc att tca ctg gac aac ggc act gtt gtc atg   3792
Gly Ser Asp Val Phe Ser Ile Ser Leu Asp Asn Gly Thr Val Val Met
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gac gta aag ggc atc aag gtc atg tca aca gac aag cag tac cac gat   3840
Asp Val Lys Gly Ile Lys Val Met Ser Thr Asp Lys Gln Tyr His Asp
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ggg ctg ccc cac ttc gtg gtc acc tcc atc tca gac aca aga tat gaa   3888
Gly Leu Pro His Phe Val Val Thr Ser Ile Ser Asp Thr Arg Tyr Glu
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ctg gta gta gac aaa agc cga ctt cga ggg aag aat cca aca aaa ggg   3936
Leu Val Val Asp Lys Ser Arg Leu Arg Gly Lys Asn Pro Thr Lys Gly
          1300                1305                1310

aag gca gag cag act caa aca act gag aag aag ttc tac ttt ggt ggc   3984
Lys Ala Glu Gln Thr Gln Thr Thr Glu Lys Lys Phe Tyr Phe Gly Gly
       1315                1320                1325

tca ccc atc agt cct cag tat gct aat ttc act gga tgt ata agc aat   4032
Ser Pro Ile Ser Pro Gln Tyr Ala Asn Phe Thr Gly Cys Ile Ser Asn
   1330                1335                1340

gcc tac ttt acc agg ttg gat aga gat gtg gaa gtc gaa gac ttc cag   4080
Ala Tyr Phe Thr Arg Leu Asp Arg Asp Val Glu Val Glu Asp Phe Gln
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cgc tat tct gaa aag gtc cac act tca ctc tat gag tgt ccg att gag   4128
Arg Tyr Ser Glu Lys Val His Thr Ser Leu Tyr Glu Cys Pro Ile Glu
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tcg tca cct ctg ttt ctc ctt cac aaa aaa gga aag aat tcc tca aag   4176
Ser Ser Pro Leu Phe Leu Leu His Lys Lys Gly Lys Asn Ser Ser Lys
          1380                1385                1390
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cct aaa aca aac aaa cag gga gag aag agt aag gat gcg cct tca tgg   4224
Pro Lys Thr Asn Lys Gln Gly Glu Lys Ser Lys Asp Ala Pro Ser Trp
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gat cct att ggc ctg aag ttt ctg gaa cag aaa gct cca aga gat tcc   4272
Asp Pro Ile Gly Leu Lys Phe Leu Glu Gln Lys Ala Pro Arg Asp Ser
   1410                1415                1420

cac tgc cac ctc tcc agc agc ccc agg gca ata gaa cat gcc tat caa   4320
His Cys His Leu Ser Ser Ser Pro Arg Ala Ile Glu His Ala Tyr Gln
1425                1430                1435                1440

tat ggc ggc acg gcc aac agt cgc cag gag ttt gaa cac gaa caa gga   4368
Tyr Gly Gly Thr Ala Asn Ser Arg Gln Glu Phe Glu His Glu Gln Gly
               1445                1450                1455

gat ttt ggt gaa aaa tcc cag ttt gcc att cgt ctg aag acc cgt tcc   4416
Asp Phe Gly Glu Lys Ser Gln Phe Ala Ile Arg Leu Lys Thr Arg Ser
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tca cat ggg atg att ttc tat gtc tca gac caa gaa gag aat gat ttc   4464
Ser His Gly Met Ile Phe Tyr Val Ser Asp Gln Glu Glu Asn Asp Phe
      1475                1480                1485

atg acc ctg ttc ttg gcc cat ggt cgc ttg gtc ttt atg ttt aat gtt   4512
Met Thr Leu Phe Leu Ala His Gly Arg Leu Val Phe Met Phe Asn Val
   1490                1495                1500

ggc cat aag aaa ctg aag att aga agc cag gag aaa tac aat gat gga   4560
Gly His Lys Lys Leu Lys Ile Arg Ser Gln Glu Lys Tyr Asn Asp Gly
1505                1510                1515                1520

ttg tgg cat gat gtg ata ttt att cgg gaa aag agc agt ggt cga ctg   4608
Leu Trp His Asp Val Ile Phe Ile Arg Glu Lys Ser Ser Gly Arg Leu
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gtc att gat ggt cta cga gtc cta gaa gaa agg ctt ccc cct agt ggc   4656
Val Ile Asp Gly Leu Arg Val Leu Glu Glu Arg Leu Pro Pro Ser Gly
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gct gcc tgg aaa atc aag ggt ccc att tat ctg gga gga gtg gct ccc   4704
Ala Ala Trp Lys Ile Lys Gly Pro Ile Tyr Leu Gly Gly Val Ala Pro
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gga aga gcc gtg aaa aat gtc cag att acc tcc gtc tac agc ttc agt   4752
Gly Arg Ala Val Lys Asn Val Gln Ile Thr Ser Val Tyr Ser Phe Ser
   1570                1575                1580

ggc tgc ctt ggc aat ctc cag ctc aat ggt gcc tcc atc acc tcc gct   4800
Gly Cys Leu Gly Asn Leu Gln Leu Asn Gly Ala Ser Ile Thr Ser Ala
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tct caa acg ttt agc gtg acc cct tgc ttt gaa ggg cca atg gaa aca   4848
Ser Gln Thr Phe Ser Val Thr Pro Cys Phe Glu Gly Pro Met Glu Thr
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gga act tat ttt tcc aca gaa ggc ggc tat gtg gtt cta gat gag tct   4896
Gly Thr Tyr Phe Ser Thr Glu Gly Gly Tyr Val Val Leu Asp Glu Ser
          1620                1625                1630

ttc aat att ggg tta aaa ttt gaa att gcc ttt gaa gtc cgc ccc cgg   4944
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Phe Asn Ile Gly Leu Lys Phe Glu Ile Ala Phe Glu Val Arg Pro Arg
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agc agt tct gga acc ctt gtc cat ggc cac agc gtc aac ggg gaa tac   4992
Ser Ser Ser Gly Thr Leu Val His Gly His Ser Val Asn Gly Glu Tyr
   1650                1655                1660

ctg aac gtg cac atg aga aac gga cag gtc ata gtg aag gtc aac aac   5040
Leu Asn Val His Met Arg Asn Gly Gln Val Ile Val Lys Val Asn Asn
1665                1670                1675                1680

ggt gtc aga gac ttt tct acc tca gta act ccc aag cag aat ctc tgt   5088
Gly Val Arg Asp Phe Ser Thr Ser Val Thr Pro Lys Gln Asn Leu Cys
               1685                1690                1695

gat ggc aga tgg cac aga att aca gtt att aga gat tca aac gtg gtt   5136
Asp Gly Arg Trp His Arg Ile Thr Val Ile Arg Asp Ser Asn Val Val
          1700                1705                1710

cag ttg gat gta gac tca gaa gtg aac cat gta gtt ggg ccg ttg aat   5184
Gln Leu Asp Val Asp Ser Glu Val Asn His Val Val Gly Pro Leu Asn
      1715                1720                1725

cca aag cca gtt gat cac agg gag cct gtg ttt gtt gga ggt gtt cca   5232
Pro Lys Pro Val Asp His Arg Glu Pro Val Phe Val Gly Gly Val Pro
   1730                1735                1740

gag tct tta ctg aca cca cgt ttg gct ccc agc aaa ccc ttc acc ggc   5280
Glu Ser Leu Leu Thr Pro Arg Leu Ala Pro Ser Lys Pro Phe Thr Gly
1745                1750                1755                1760

tgc atc cgc cac ttt gta att gac agc cgc cct gtg agc ttc agt aaa   5328
Cys Ile Arg His Phe Val Ile Asp Ser Arg Pro Val Ser Phe Ser Lys
               1765                1770                1775

gct gcc ctg gtc agt ggt gct gtg agc atc aac tcc tgt ccc aca gcc   5376
Ala Ala Leu Val Ser Gly Ala Val Ser Ile Asn Ser Cys Pro Thr Ala
          1780                1785                1790

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         35                  40                  45
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Arg Thr Leu Ser Gly Glu Cys Ala Pro Cys Asp Cys Asn Gly Asn Ser
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His Glu Cys Leu Asp Gly Ser Gly Phe Cys Leu His Cys Gln Arg Asn
 65                  70                  75                  80

Thr Thr Gly Glu His Cys Glu Lys Cys Leu Asp Gly Tyr Ile Gly Asp
                 85                  90                  95

Ser Ile Arg Gly Thr Pro Arg Phe Cys Gln Pro Cys Pro Cys Pro Leu
            100                 105                 110

Pro His Leu Ala Asn Phe Ala Glu Ser Cys Tyr Arg Lys Asn Gly Ala
        115                 120                 125

Val Arg Cys Ile Cys Lys Glu Asn Tyr Val Gly Pro Asn Cys Glu Arg
    130                 135                 140

Cys Ala Pro Gly Tyr Tyr Gly Asn Pro Leu Leu Ile Gly Ser Thr Cys
145                 150                 155                 160

Lys Lys Cys Asp Cys Ser Gly Asn Ser Asp Pro Asn Leu Ile Phe Glu
                165                 170                 175

Asp Cys Asp Glu Ile Thr Gly Gln Cys Arg Asn Cys Leu Arg Asn Thr
            180                 185                 190

Thr Gly Phe Lys Cys Glu Arg Cys Ala Pro Gly Tyr Tyr Gly Asp Ala
        195                 200                 205

Arg Thr Ala Lys Asn Cys Ala Val Cys Asn Cys Gly Gly Gly Pro Arg
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Asp Ser Val Thr Gly Glu Cys Leu Glu Glu Gly Phe Glu Val Pro Thr
225                 230                 235                 240

Gly Cys Asp Lys Cys Val Trp Asp Leu Thr Asp Asp Leu Arg Leu Ala
                245                 250                 255

Ala Leu Ser Ile Glu Glu Ser Lys Ser Gly Leu Leu Ser Val Ser Ser
            260                 265                 270

Ala Ala Ala Ala His Arg His Val Thr Asp Met Asn Ser Thr Ile His
        275                 280                 285

Leu Leu Arg Thr Arg Leu Ser Glu Arg Glu Asn Gln Tyr Thr Leu Arg
    290                 295                 300

Lys Ile Gln Ile Asn Asn Ser Glu Asn Thr Leu Arg Ser Leu Leu Pro
305                 310                 315                 320

Asp Val Glu Gly Leu His Glu Lys Gly Ser Gln Ala Ser Arg Lys Gly
                325                 330                 335

Met Leu Val Glu Lys Glu Ser Met Asp Thr Ile Asp Gln Ala Thr His
            340                 345                 350

Leu Val Glu Gln Ala His Asn Met Arg Asp Lys Ile Gln Glu Ile Asn
        355                 360                 365

Ser Lys Met Leu Tyr Tyr Gly Glu Asn Gln Glu Leu Gly Pro Glu Glu
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    370                 375                 380

Ile Ala Glu Lys Leu Val Leu Ala Gln Lys Met Leu Glu Glu Ile Arg
385                 390                 395                 400

Ser Arg Gln Pro Phe Leu Thr His Arg Glu Leu Val Asp Glu Glu Ala
                405                 410                 415

Asp Glu Ala Gln Glu Leu Leu Ser Gln Ala Glu Asn Trp Gln Arg Leu
            420                 425                 430

His Asn Asp Thr Arg Ser Leu Phe Pro Val Val Leu Glu Gln Leu Asp
        435                 440                 445

Asp Tyr Asn Ala Lys Leu Ser Asp Leu Gln Glu Ser Ile Asn Gln Ala
    450                 455                 460

Leu Asp His Val Arg Asp Ala Glu Asp Met Asn Arg Ala Ile Thr Phe
465                 470                 475                 480

Lys Gln Arg Asp His Glu Lys Gln His Glu Arg Val Lys Glu Gln Met
                485                 490                 495

Glu Val Val Gly Ala Ser Leu Ser Met Ser Ala Asp Ser Leu Thr Ile
            500                 505                 510

Pro Gln Leu Thr Leu Glu Glu Leu Asp Glu Ile Ile Lys Asn Ala Ser
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Gly Ile Tyr Ala Glu Ile Asp Gly Ala Lys Asn Glu Leu Gln Gly Lys
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Leu Ser Asn Leu Ser Asn Leu Ser His Asp Leu Val Gln Glu Ala Thr
545                 550                 555                 560

Asp His Ala Tyr Asn Leu Gln Gln Glu Ala Asp Glu Leu Ser Arg Asn
                565                 570                 575

Leu His Ser Ser Asp Met Asn Gly Leu Val Gln Lys Ala Leu Asp Ala
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Ser Asn Val Tyr Glu Asn Ile Ala Asn Tyr Val Ser Glu Ala Asn Glu
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Thr Ala Glu Leu Ala Leu Asn Ile Thr Asp Arg Ile Tyr Asp Ala Val
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Ser Gly Ile Asp Thr Gln Ile Ile Tyr His Lys Asp Glu Ser Asp Asn
625                 630                 635                 640

Leu Leu Asn Gln Ala Arg Glu Leu Gln Ala Lys Ala Asp Ser Cys Asn
                645                 650                 655

Asp Glu Ala Val Ala Asp Thr Ser Arg Arg Val Gly Gly Ala Leu Trp
            660                 665                 670

Arg Lys Gly Ala Leu Arg Asp Arg Leu Asn Asp Ala Val Lys Gln Leu
        675                 680                 685

Gln Ala Ala Glu Arg Gly Asp Ala His Gln Arg Leu Gly Gln Ser Lys
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Leu Phe Ile Glu Glu Ala Asn Lys Thr Thr Ala Ala Val Gln Gln Val
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Thr Thr Pro Met Ala Asn Asn Leu Ser Asn Trp Ser Gln Asn Leu Gln
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Thr Phe Asp Ser Ser Ala Tyr Asn Thr Ala Val Asp Ser Ala Arg Asp
            740                 745                 750

Ala Val Arg Asn Leu Thr Glu Val Val Pro Gln Leu Leu Asp Gln Leu
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Arg Thr Val Glu Gln Lys Arg Pro Ala Ser Asn Ile Ser Ala Ser Ile
    770                 775                 780

Gln Ser Ile Arg Glu Leu Ile Ala Gln Thr Arg Ser Val Ala Ser Lys
785                 790                 795                 800

Ile Gln Val Ser Met Met Phe Asp Gly Gln Ser Ala Val Glu Val His
                805                 810                 815

Pro Lys Val Ser Val Asp Asp Leu Lys Ala Phe Thr Ser Ile Ser Leu
            820                 825                 830

Tyr Met Lys Pro Pro Pro Lys Pro Ala Glu Pro Thr Gly Ala Trp Val
        835                 840                 845

Ala Asp Gln Phe Val Leu Tyr Leu Gly Ser Lys Asn Ala Lys Lys Glu
    850                 855                 860

Tyr Met Gly Leu Ala Ile Lys Asn Asp Asn Leu Val Tyr Val Tyr Asn
865                 870                 875                 880

Leu Gly Met Lys Asp Val Glu Ile Leu Leu Asp Ser Lys Pro Val Ser
                885                 890                 895

Ser Trp Pro Ala Tyr Phe Ser Ile Val Lys Ile Glu Arg Val Gly Glu
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His Gly Lys Val Phe Leu Thr Val Pro Ser Leu Ser Ser Thr Ala Glu
        915                 920                 925

Glu Lys Phe Ile Lys Lys Gly Glu Phe Ala Gly Asp Asp Ser Leu Leu
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Asp Val Thr Pro Glu Asp Thr Val Phe Tyr Val Gly Gly Val Pro Ala
945                 950                 955                 960

Asn Phe Lys Leu Pro Ala Ser Leu Asn Leu Pro Ser Tyr Ser Gly Cys
                965                 970                 975

Leu Glu Leu Ala Thr Leu Asn Asn Asp Val Ile Ser Leu Tyr Asn Phe
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Lys His Ile Tyr Asn Met Asp Pro Ser Lys Ser Val Pro Cys Ala Arg
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Ala Lys Tyr His Glu Ile Ser Ile Ile Tyr His Asn Asp Lys Lys Met
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Lys Lys Ile Pro Phe Thr Asp Ile Tyr Ile Gly Gly Ala Pro Gln Glu
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Leu Val Val Asp Lys Ser Arg Leu Arg Gly Lys Asn Pro Thr Lys Gly
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Arg Tyr Ser Glu Lys Val His Thr Ser Leu Tyr Glu Cys Pro Ile Glu
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Ser Ser Pro Leu Phe Leu Leu His Lys Lys Gly Lys Asn Ser Ser Lys
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Asp Pro Ile Gly Leu Lys Phe Leu Glu Gln Lys Ala Pro Arg Asp Ser
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His Cys His Leu Ser Ser Ser Pro Arg Ala Ile Glu His Ala Tyr Gln
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Tyr Gly Gly Thr Ala Asn Ser Arg Gln Glu Phe Glu His Glu Gln Gly
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Met Thr Leu Phe Leu Ala His Gly Arg Leu Val Phe Met Phe Asn Val
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Phe Asn Ile Gly Leu Lys Phe Glu Ile Ala Phe Glu Val Arg Pro Arg
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Gln Leu Asp Val Asp Ser Glu Val Asn His Val Val Gly Pro Leu Asn
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Glu Ser Leu Leu Thr Pro Arg Leu Ala Pro Ser Lys Pro Phe Thr Gly
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Cys Ile Arg His Phe Val Ile Asp Ser Arg Pro Val Ser Phe Ser Lys
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Gly Ser Cys Tyr Pro Ala Thr Gly Asp Leu Leu Ile Gly Arg Ala Gln
         35                  40                  45

aag ctt tcg gtg acc tcg acg tgc ggg ctg cac aag ccc gaa ccc tac   309
Lys Leu Ser Val Thr Ser Thr Cys Gly Leu His Lys Pro Glu Pro Tyr
     50                  55                  60

tgt atc gtc agc cac ttg cag gag gac aaa aaa tgc ttc ata tgc aat   357
Cys Ile Val Ser His Leu Gln Glu Asp Lys Lys Cys Phe Ile Cys Asn
 65                  70                  75                  80
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tcc caa gat cct tat cat gag acc ctg aat cct gac agc cat ctc att   405
Ser Gln Asp Pro Tyr His Glu Thr Leu Asn Pro Asp Ser His Leu Ile
                 85                  90                  95

gaa aat gtg gtc act aca ttt gct cca aac cgc ctt aag att tgg tgg   453
Glu Asn Val Val Thr Thr Phe Ala Pro Asn Arg Leu Lys Ile Trp Trp
            100                 105                 110

caa tct gaa aat ggt gtg gaa aat gta act atc caa ctg gat ttg gaa   501
Gln Ser Glu Asn Gly Val Glu Asn Val Thr Ile Gln Leu Asp Leu Glu
        115                 120                 125

gca gaa ttc cat ttt act cat ctc ata atg act ttc aag aca ttc cgt   549
Ala Glu Phe His Phe Thr His Leu Ile Met Thr Phe Lys Thr Phe Arg
    130                 135                 140

cca gct gct atg ctg ata gaa cga tcg tcc gac ttt ggg aaa acc tgg   597
Pro Ala Ala Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp
145                 150                 155                 160

ggt gtg tat aga tac ttc gcc tat gac tgt gag gcc tcg ttt cca ggc   645
Gly Val Tyr Arg Tyr Phe Ala Tyr Asp Cys Glu Ala Ser Phe Pro Gly
                165                 170                 175

att tca act ggc ccc atg aaa aaa gtc gat gac ata att tgt gat tct   693
Ile Ser Thr Gly Pro Met Lys Lys Val Asp Asp Ile Ile Cys Asp Ser
            180                 185                 190

cga tat tct gac att gaa ccc tca act gaa gga gag gtg ata ttt cgt   741
Arg Tyr Ser Asp Ile Glu Pro Ser Thr Glu Gly Glu Val Ile Phe Arg
        195                 200                 205

gct tta gat cct gct ttc aaa ata gaa gat cct tat agc cca agg ata   789
Ala Leu Asp Pro Ala Phe Lys Ile Glu Asp Pro Tyr Ser Pro Arg Ile
    210                 215                 220

cag aat tta tta aaa att acc aac ttg aga atc aag ttt gtg aaa ctg   837
Gln Asn Leu Leu Lys Ile Thr Asn Leu Arg Ile Lys Phe Val Lys Leu
225                 230                 235                 240

cat act ttg gga gat aac ctt ctg gat tcc agg atg gaa atc aga gaa   885
His Thr Leu Gly Asp Asn Leu Leu Asp Ser Arg Met Glu Ile Arg Glu
                245                 250                 255

aag tat tat tat gca gtt tat gat atg gtg gtt cga gga aat tgc ttc   933
Lys Tyr Tyr Tyr Ala Val Tyr Asp Met Val Val Arg Gly Asn Cys Phe
            260                 265                 270

tgc tat ggt cat gcc agc gaa tgt gcc cct gtg gat gga ttc aat gaa   981
Cys Tyr Gly His Ala Ser Glu Cys Ala Pro Val Asp Gly Phe Asn Glu
        275                 280                 285

gaa gtg gaa gga atg gtt cac gga cac tgc atg tgc agg cat aac acc   1029
Glu Val Glu Gly Met Val His Gly His Cys Met Cys Arg His Asn Thr
    290                 295                 300

aag ggc tta aac tgt gaa ctc tgc atg gat ttc tac cat gat tta cct   1077
Lys Gly Leu Asn Cys Glu Leu Cys Met Asp Phe Tyr His Asp Leu Pro
305                 310                 315                 320

tgg aga cct gct gaa ggc cga aac agc aac gcc tgt aaa aaa tgt aac   1125
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Trp Arg Pro Ala Glu Gly Arg Asn Ser Asn Ala Cys Lys Lys Cys Asn
                325                 330                 335

tgc aat gaa cat tcc atc tct tgt cac ttt gac atg gct gtt tac ctg   1173
Cys Asn Glu His Ser Ile Ser Cys His Phe Asp Met Ala Val Tyr Leu
            340                 345                 350

gcc acg ggg aac gtc agc gga ggc gtg tgt gat gac tgt cag cac aac   1221
Ala Thr Gly Asn Val Ser Gly Gly Val Cys Asp Asp Cys Gln His Asn
        355                 360                 365

acc atg ggg cgc aac tgt gag cag tgc aag ccg ttt tac tac cag cac   1269
Thr Met Gly Arg Asn Cys Glu Gln Cys Lys Pro Phe Tyr Tyr Gln His
    370                 375                 380

cca gag agg gac atc cga gat cct aat ttc tgt gaa cga tgt acg tgt   1317
Pro Glu Arg Asp Ile Arg Asp Pro Asn Phe Cys Glu Arg Cys Thr Cys
385                 390                 395                 400

gac cca gct ggc tct caa aat gag gga att tgt gac agc tat act gat   1365
Asp Pro Ala Gly Ser Gln Asn Glu Gly Ile Cys Asp Ser Tyr Thr Asp
                405                 410                 415

ttt tct act ggt ctc att gct ggc cag tgt cgg tgt aaa tta aat gtg   1413
Phe Ser Thr Gly Leu Ile Ala Gly Gln Cys Arg Cys Lys Leu Asn Val
            420                 425                 430

gaa gga gaa cat tgt gat gtt tgc aaa gaa ggc ttc tat gat tta agc   1461
Glu Gly Glu His Cys Asp Val Cys Lys Glu Gly Phe Tyr Asp Leu Ser
        435                 440                 445

agt gaa gat cca ttt ggt tgt aaa tct tgt gct tgc aat cct ctg gga   1509
Ser Glu Asp Pro Phe Gly Cys Lys Ser Cys Ala Cys Asn Pro Leu Gly
    450                 455                 460

aca att cct gga ggg aat cct tgt gat tcc gag aca ggt cac tgc tac   1557
Thr Ile Pro Gly Gly Asn Pro Cys Asp Ser Glu Thr Gly His Cys Tyr
465                 470                 475                 480

tgc aag cgt ctg gtg aca gga cag cat tgt gac cag tgc ctg cca gag   1605
Cys Lys Arg Leu Val Thr Gly Gln His Cys Asp Gln Cys Leu Pro Glu
                485                 490                 495

cac tgg ggc tta agc aat gat ttg gat gga tgt cga cca tgt gac tgt   1653
His Trp Gly Leu Ser Asn Asp Leu Asp Gly Cys Arg Pro Cys Asp Cys
            500                 505                 510

gac ctt ggg gga gcc tta aac aac agt tgc ttt gcg gag tca ggc cag   1701
Asp Leu Gly Gly Ala Leu Asn Asn Ser Cys Phe Ala Glu Ser Gly Gln
        515                 520                 525

tgc tca tgc cgg cct cac atg att gga cgt cag tgc aac gaa gtg gaa   1749
Cys Ser Cys Arg Pro His Met Ile Gly Arg Gln Cys Asn Glu Val Glu
    530                 535                 540

cct ggt tac tac ttt gcc acc ctg gat cac tac ctc tat gaa gcg gag   1797
Pro Gly Tyr Tyr Phe Ala Thr Leu Asp His Tyr Leu Tyr Glu Ala Glu
545                 550                 555                 560

gaa gcc aac ttg ggg cct ggg gtt agc ata gtg gag cgg caa tat atc   1845
Glu Ala Asn Leu Gly Pro Gly Val Ser Ile Val Glu Arg Gln Tyr Ile
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                565                 570                 575

cag gac cgg att ccc tcc tgg act gga gcc ggc ttc gtc cga gtg cct   1893
Gln Asp Arg Ile Pro Ser Trp Thr Gly Ala Gly Phe Val Arg Val Pro
            580                 585                 590

gaa ggg gct tat ttg gag ttt ttc att gac aac ata cca tat tcc atg   1941
Glu Gly Ala Tyr Leu Glu Phe Phe Ile Asp Asn Ile Pro Tyr Ser Met
        595                 600                 605

gag tac gac atc cta att cgc tac gag cca cag cta ccc gac cac tgg   1989
Glu Tyr Asp Ile Leu Ile Arg Tyr Glu Pro Gln Leu Pro Asp His Trp
    610                 615                 620

gaa aaa gct gtc atc aca gtg cag cga cct gga agg att cca acc agc   2037
Glu Lys Ala Val Ile Thr Val Gln Arg Pro Gly Arg Ile Pro Thr Ser
625                 630                 635                 640

agc cga tgt ggt aat acc atc ccc gat gat gac aac cag gtg gtg tca   2085
Ser Arg Cys Gly Asn Thr Ile Pro Asp Asp Asp Asn Gln Val Val Ser
                645                 650                 655

tta tca cca ggc tca aga tat gtc gtc ctt cct cgg ccg gtg tgc ttt   2133
Leu Ser Pro Gly Ser Arg Tyr Val Val Leu Pro Arg Pro Val Cys Phe
            660                 665                 670

gag aag gga aca aac tac acg gtg agg ttg gag ctg cct cag tac acc   2181
Glu Lys Gly Thr Asn Tyr Thr Val Arg Leu Glu Leu Pro Gln Tyr Thr
        675                 680                 685

tcc tct gat agc gac gtg gag agc ccc tac acg ctg atc gat tct ctt   2229
Ser Ser Asp Ser Asp Val Glu Ser Pro Tyr Thr Leu Ile Asp Ser Leu
    690                 695                 700

gtt ctc atg cca tac tgt aaa tca ctg gac atc ttc acc gtg gga ggt   2277
Val Leu Met Pro Tyr Cys Lys Ser Leu Asp Ile Phe Thr Val Gly Gly
705                 710                 715                 720

tca gga gat ggg gtg gtc acc aac agt gcc tgg gaa acc ttt cag aga   2325
Ser Gly Asp Gly Val Val Thr Asn Ser Ala Trp Glu Thr Phe Gln Arg
                725                 730                 735

tac cga tgt cta gag aac agc aga agc gtt gtg aaa aca ccg atg aca   2373
Tyr Arg Cys Leu Glu Asn Ser Arg Ser Val Val Lys Thr Pro Met Thr
            740                 745                 750

gat gtt tgc aga aac atc atc ttt agc att tct gcc ctg tta cac cag   2421
Asp Val Cys Arg Asn Ile Ile Phe Ser Ile Ser Ala Leu Leu His Gln
        755                 760                 765

aca ggc ctg gct tgt gaa tgc gac cct cag ggt tcg tta agt tcc gtg   2469
Thr Gly Leu Ala Cys Glu Cys Asp Pro Gln Gly Ser Leu Ser Ser Val
    770                 775                 780

tgt gat ccc aac gga ggc cag tgc cag tgc cgg ccc aac gtg gtt gga   2517
Cys Asp Pro Asn Gly Gly Gln Cys Gln Cys Arg Pro Asn Val Val Gly
785                 790                 795                 800

aga acc tgc aac aga tgt gca cct gga act ttt ggc ttt ggc ccc agt   2565
Arg Thr Cys Asn Arg Cys Ala Pro Gly Thr Phe Gly Phe Gly Pro Ser
                805                 810                 815
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gga tgc aaa cct tgt gag tgc cat ctg caa gga tct gtc aat gcc ttc   2613
Gly Cys Lys Pro Cys Glu Cys His Leu Gln Gly Ser Val Asn Ala Phe
            820                 825                 830

tgc aat ccc gtc act ggc cag tgc cac tgt ttc cag gga gtg tat gct   2661
Cys Asn Pro Val Thr Gly Gln Cys His Cys Phe Gln Gly Val Tyr Ala
        835                 840                 845

cgg cag tgt gat cgg tgc tta cct ggg cac tgg ggc ttt cca agt tgc   2709
Arg Gln Cys Asp Arg Cys Leu Pro Gly His Trp Gly Phe Pro Ser Cys
    850                 855                 860

cag ccc tgc cag tgc aat ggc cac gcc gat gac tgc gac cca gtg act   2757
Gln Pro Cys Gln Cys Asn Gly His Ala Asp Asp Cys Asp Pro Val Thr
865                 870                 875                 880

ggg gag tgc ttg aac tgc cag gac tac acc atg ggt cat aac tgt gaa   2805
Gly Glu Cys Leu Asn Cys Gln Asp Tyr Thr Met Gly His Asn Cys Glu
                885                 890                 895

agg tgc ttg gct ggt tac tat ggc gac ccc atc att ggg tca ggt gat   2853
Arg Cys Leu Ala Gly Tyr Tyr Gly Asp Pro Ile Ile Gly Ser Gly Asp
            900                 905                 910

cac tgc cgc cct tgc cct tgc cca gat ggt ccc gac agt gga cgc cag   2901
His Cys Arg Pro Cys Pro Cys Pro Asp Gly Pro Asp Ser Gly Arg Gln
        915                 920                 925

ttt gcc agg agc tgc tac caa gat cct gtt act tta cag ctt gcc tgt   2949
Phe Ala Arg Ser Cys Tyr Gln Asp Pro Val Thr Leu Gln Leu Ala Cys
    930                 935                 940

gtt tgt gat cct gga tac att ggt tcc aga tgt gac gac tgt gcc tca   2997
Val Cys Asp Pro Gly Tyr Ile Gly Ser Arg Cys Asp Asp Cys Ala Ser
945                 950                 955                 960

gga tac ttt ggc aat cca tca gaa gtt ggg ggg tcg tgt cag cct tgc   3045
Gly Tyr Phe Gly Asn Pro Ser Glu Val Gly Gly Ser Cys Gln Pro Cys
                965                 970                 975

cag tgt cac aac aac att gac acg aca gac cca gaa gcc tgt gac aag   3093
Gln Cys His Asn Asn Ile Asp Thr Thr Asp Pro Glu Ala Cys Asp Lys
            980                 985                 990

gag act ggg agg tgt ctc aag tgc ctg tac cac acg gaa ggg gaa cac   3141
Glu Thr Gly Arg Cys Leu Lys Cys Leu Tyr His Thr Glu Gly Glu His
        995                1000                1005

tgt cag ttc tgc cgg ttt gga tac tat ggt gat gcc ctc cgg cag gac   3189
Cys Gln Phe Cys Arg Phe Gly Tyr Tyr Gly Asp Ala Leu Arg Gln Asp
   1010                1015                1020

tgt cga aag tgt gtc tgt aat tac ctg ggc acc gtg caa gag cac tgt   3237
Cys Arg Lys Cys Val Cys Asn Tyr Leu Gly Thr Val Gln Glu His Cys
1025                1030                1035                1040

aac ggc tct gac tgc cag tgc gac aaa gcc act ggt cag tgc ttg tgt   3285
Asn Gly Ser Asp Cys Gln Cys Asp Lys Ala Thr Gly Gln Cys Leu Cys
               1045                1050                1055
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ctt cct aat gtg atc ggg cag aac tgt gac cgc tgt gcg ccc aat acc   3333
Leu Pro Asn Val Ile Gly Gln Asn Cys Asp Arg Cys Ala Pro Asn Thr
          1060                1065                1070

tgg cag ctg gcc agt ggc act ggc tgt gac cca tgc aac tgc aat gct   3381
Trp Gln Leu Ala Ser Gly Thr Gly Cys Asp Pro Cys Asn Cys Asn Ala
      1075                1080                1085

gct cat tcc ttc ggg cca tct tgc aat gag ttc acg ggg cag tgc cag   3429
Ala His Ser Phe Gly Pro Ser Cys Asn Glu Phe Thr Gly Gln Cys Gln
  1090                1095                1100

tgc atg cct ggg ttt gga ggc cgc acc tgc agc gag tgc cag gaa ctc   3477
Cys Met Pro Gly Phe Gly Gly Arg Thr Cys Ser Glu Cys Gln Glu Leu
1105                1110                1115                1120

ttc tgg gga gac ccc gac gtg gag tgc cga gcc tgt gac tgt gac ccc   3525
Phe Trp Gly Asp Pro Asp Val Glu Cys Arg Ala Cys Asp Cys Asp Pro
              1125                1130                1135

agg ggc att gag acg cca cag tgt gac cag tcc acg ggc cag tgt gtc   3573
Arg Gly Ile Glu Thr Pro Gln Cys Asp Gln Ser Thr Gly Gln Cys Val
          1140                1145                1150

tgc gtt gag ggt gtt gag ggt cca cgc tgt gac aag tgc acg cga ggg   3621
Cys Val Glu Gly Val Glu Gly Pro Arg Cys Asp Lys Cys Thr Arg Gly
      1155                1160                1165

tac tcg ggg gtc ttc cct gac tgc aca ccc tgc cac cag tgc ttt gct   3669
Tyr Ser Gly Val Phe Pro Asp Cys Thr Pro Cys His Gln Cys Phe Ala
  1170                1175                1180

ctc tgg gat gtg atc att gcc gag ctg acc aac agg aca cac aga ttc   3717
Leu Trp Asp Val Ile Ile Ala Glu Leu Thr Asn Arg Thr His Arg Phe
1185                1190                1195                1200

ctg gag aaa gcc aag gcc ttg aag atc agt ggt gtg atc ggg cct tac   3765
Leu Glu Lys Ala Lys Ala Leu Lys Ile Ser Gly Val Ile Gly Pro Tyr
              1205                1210                1215

cgt gag act gtg gac tcg gtg gag agg aaa gtc agc gag ata aaa gac   3813
Arg Glu Thr Val Asp Ser Val Glu Arg Lys Val Ser Glu Ile Lys Asp
          1220                1225                1230

atc ctg gcg cag agc ccc gca gca gag cca ctg aaa aac att ggg aat   3861
Ile Leu Ala Gln Ser Pro Ala Ala Glu Pro Leu Lys Asn Ile Gly Asn
      1235                1240                1245

ctc ttt gag gaa gca gag aaa ctg att aaa gat gtt aca gaa atg atg   3909
Leu Phe Glu Glu Ala Glu Lys Leu Ile Lys Asp Val Thr Glu Met Met
  1250                1255                1260

gct caa gta gaa gtg aaa tta tct gac aca act tcc caa agc aac agc   3957
Ala Gln Val Glu Val Lys Leu Ser Asp Thr Thr Ser Gln Ser Asn Ser
1265                1270                1275                1280

aca gcc aaa gaa ctg gat tct cta cag aca gaa gcc gaa agc cta gac   4005
Thr Ala Lys Glu Leu Asp Ser Leu Gln Thr Glu Ala Glu Ser Leu Asp
              1285                1290                1295

aac act gtg aaa gaa ctt gct gaa caa ctg gaa ttt atc aaa aac tca   4053
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Asn Thr Val Lys Glu Leu Ala Glu Gln Leu Glu Phe Ile Lys Asn Ser
          1300                1305                1310

gat att cgg ggt gcc ttg gat agc att acc aag tat ttc cag atg tct   4101
Asp Ile Arg Gly Ala Leu Asp Ser Ile Thr Lys Tyr Phe Gln Met Ser
      1315                1320                1325

ctt gag gca gag gag agg gtg aat gcc tcc acc aca gaa ccc aac agc   4149
Leu Glu Ala Glu Glu Arg Val Asn Ala Ser Thr Thr Glu Pro Asn Ser
   1330                1335                1340

act gtg gag cag tca gcc ctc atg aga gac aga gta gaa gac gtg atg   4197
Thr Val Glu Gln Ser Ala Leu Met Arg Asp Arg Val Glu Asp Val Met
1345                1350                1355                1360

atg gag cga gaa tcc cag ttc aag gaa aaa caa gag gag cag gct cgc   4245
Met Glu Arg Glu Ser Gln Phe Lys Glu Lys Gln Glu Glu Gln Ala Arg
               1365                1370                1375

ctc ctt gat gaa ctg gca ggc aag cta caa agc cta gac ctt tca gcc   4293
Leu Leu Asp Glu Leu Ala Gly Lys Leu Gln Ser Leu Asp Leu Ser Ala
          1380                1385                1390

gct gcc gaa atg acc tgt gga aca ccc cca ggg gcc tcc tgt tcc gag   4341
Ala Ala Glu Met Thr Cys Gly Thr Pro Pro Gly Ala Ser Cys Ser Glu
      1395                1400                1405

act gaa tgt ggc ggg cca aac tgc aga act gac gaa gga gag agg aag   4389
Thr Glu Cys Gly Gly Pro Asn Cys Arg Thr Asp Glu Gly Glu Arg Lys
   1410                1415                1420

tgt ggg ggg cct ggc tgt ggt ggt ctg gtt act gtt gca cac aac gcc   4437
Cys Gly Gly Pro Gly Cys Gly Gly Leu Val Thr Val Ala His Asn Ala
1425                1430                1435                1440

tgg cag aaa gcc atg gac ttg gac caa gat gtc ctg agt gcc ctg gct   4485
Trp Gln Lys Ala Met Asp Leu Asp Gln Asp Val Leu Ser Ala Leu Ala
               1445                1450                1455

gaa gtg gaa cag ctc tcc aag atg gtc tct gaa gca aaa ctg agg gca   4533
Glu Val Glu Gln Leu Ser Lys Met Val Ser Glu Ala Lys Leu Arg Ala
          1460                1465                1470

gat gag gca aaa caa agt gct gaa gac att ctg ttg aag aca aat gct   4581
Asp Glu Ala Lys Gln Ser Ala Glu Asp Ile Leu Leu Lys Thr Asn Ala
      1475                1480                1485

acc aaa gaa aaa atg gac aag agc aat gag gag ctg aga aat cta atc   4629
Thr Lys Glu Lys Met Asp Lys Ser Asn Glu Glu Leu Arg Asn Leu Ile
   1490                1495                1500

aag caa atc aga aac ttt ttg acc cag gat agt gct gat ttg gac agc   4677
Lys Gln Ile Arg Asn Phe Leu Thr Gln Asp Ser Ala Asp Leu Asp Ser
1505                1510                1515                1520

att gaa gca gtt gct aat gaa gta ttg aaa atg gag atg cct agc acc   4725
Ile Glu Ala Val Ala Asn Glu Val Leu Lys Met Glu Met Pro Ser Thr
               1525                1530                1535

cca cag cag tta cag aac ttg aca gaa gat ata cgt gaa cga gtt gaa   4773
Pro Gln Gln Leu Gln Asn Leu Thr Glu Asp Ile Arg Glu Arg Val Glu
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          1540                1545                1550

agc ctt tct caa gta gag gtt att ctt cag cat agt gct gct gac att   4821
Ser Leu Ser Gln Val Glu Val Ile Leu Gln His Ser Ala Ala Asp Ile
       1555                1560                1565

gcc aga gct gag atg ttg tta gaa gaa gct aaa aga gca agc aaa agt   4869
Ala Arg Ala Glu Met Leu Leu Glu Glu Ala Lys Arg Ala Ser Lys Ser
   1570                1575                1580

gca aca gat gtt aaa gtc act gca gat atg gta aag gaa gct ctg gaa   4917
Ala Thr Asp Val Lys Val Thr Ala Asp Met Val Lys Glu Ala Leu Glu
1585                1590                1595                1600

gaa gca gaa aag gcc cag gtc gca gca gag aag gca att aaa caa gca   4965
Glu Ala Glu Lys Ala Gln Val Ala Ala Glu Lys Ala Ile Lys Gln Ala
               1605                1610                1615

gat gaa gac att caa gga acc cag aac ctg tta act tcg att gag tct   5013
Asp Glu Asp Ile Gln Gly Thr Gln Asn Leu Leu Thr Ser Ile Glu Ser
           1620                1625                1630

gaa aca gca gct tct gag gaa acc ttg ttc aac gcg tcc cag cgc atc   5061
Glu Thr Ala Ala Ser Glu Glu Thr Leu Phe Asn Ala Ser Gln Arg Ile
       1635                1640                1645

agc gag tta gag agg aat gtg gaa gaa ctt aag cgg aaa gct gcc caa   5109
Ser Glu Leu Glu Arg Asn Val Glu Glu Leu Lys Arg Lys Ala Ala Gln
   1650                1655                1660

aac tcc ggg gag gca gaa tat att gaa aaa gta gta tat act gtg aag   5157
Asn Ser Gly Glu Ala Glu Tyr Ile Glu Lys Val Val Tyr Thr Val Lys
1665                1670                1675                1680

caa agt gca gaa gat gtt aag aag act tta gat ggt gaa ctt gat gaa   5205
Gln Ser Ala Glu Asp Val Lys Lys Thr Leu Asp Gly Glu Leu Asp Glu
               1685                1690                1695

aag tat aaa aaa gta gaa aat tta att gcc aaa aaa act gaa gag tca   5253
Lys Tyr Lys Lys Val Glu Asn Leu Ile Ala Lys Lys Thr Glu Glu Ser
           1700                1705                1710

gct gat gcc aga agg aaa gcc gaa atg cta caa aat gaa gca aaa act   5301
Ala Asp Ala Arg Arg Lys Ala Glu Met Leu Gln Asn Glu Ala Lys Thr
       1715                1720                1725

ctt tta gct caa gca aat agc aag ctg caa ctg ctc aaa gat tta gaa   5349
Leu Leu Ala Gln Ala Asn Ser Lys Leu Gln Leu Leu Lys Asp Leu Glu
   1730                1735                1740

aga aaa tat gaa gac aat caa aga tac tta gaa gat aaa gct caa gaa   5397
Arg Lys Tyr Glu Asp Asn Gln Arg Tyr Leu Glu Asp Lys Ala Gln Glu
1745                1750                1755                1760

tta gca aga ctg gaa gga gaa gtc cgt tca ctc cta aag gat ata agc   5445
Leu Ala Arg Leu Glu Gly Glu Val Arg Ser Leu Leu Lys Asp Ile Ser
               1765                1770                1775

cag aaa gtt gct gtg tat agc aca tgc ttg taacagagga gaataaaaaa     5495
Gln Lys Val Ala Val Tyr Ser Thr Cys Leu
           1780                1785
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tggctgaggt gaacaaggta aaacaactac attttaaaaa ctgacttaat gctcttcaaa 5555

ataaaacatc acctatttaa tgtttttaat cacattttgt atgagttaaa taaagccc 5613

<210> 14
<211> 1786
<212> PRT
<213> Homo sapiens

<400> 14

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Met Gly Leu Leu Gln Leu Leu Ala Phe Ser Phe Leu Ala Leu Cys Arg
  1               5                  10                  15

Ala Arg Val Arg Ala Gln Glu Pro Glu Phe Ser Tyr Gly Cys Ala Glu
             20                  25                  30

Gly Ser Cys Tyr Pro Ala Thr Gly Asp Leu Leu Ile Gly Arg Ala Gln
         35                  40                  45

Lys Leu Ser Val Thr Ser Thr Cys Gly Leu His Lys Pro Glu Pro Tyr
     50                  55                  60

Cys Ile Val Ser His Leu Gln Glu Asp Lys Lys Cys Phe Ile Cys Asn
 65                  70                  75                  80

Ser Gln Asp Pro Tyr His Glu Thr Leu Asn Pro Asp Ser His Leu Ile
                 85                  90                  95

Glu Asn Val Val Thr Thr Phe Ala Pro Asn Arg Leu Lys Ile Trp Trp
            100                 105                 110

Gln Ser Glu Asn Gly Val Glu Asn Val Thr Ile Gln Leu Asp Leu Glu
        115                 120                 125

Ala Glu Phe His Phe Thr His Leu Ile Met Thr Phe Lys Thr Phe Arg
    130                 135                 140

Pro Ala Ala Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp
145                 150                 155                 160

Gly Val Tyr Arg Tyr Phe Ala Tyr Asp Cys Glu Ala Ser Phe Pro Gly
                165                 170                 175

Ile Ser Thr Gly Pro Met Lys Lys Val Asp Asp Ile Ile Cys Asp Ser
            180                 185                 190

Arg Tyr Ser Asp Ile Glu Pro Ser Thr Glu Gly Glu Val Ile Phe Arg
        195                 200                 205

Ala Leu Asp Pro Ala Phe Lys Ile Glu Asp Pro Tyr Ser Pro Arg Ile
    210                 215                 220

Gln Asn Leu Leu Lys Ile Thr Asn Leu Arg Ile Lys Phe Val Lys Leu
225                 230                 235                 240

His Thr Leu Gly Asp Asn Leu Leu Asp Ser Arg Met Glu Ile Arg Glu
                245                 250                 255

Lys Tyr Tyr Tyr Ala Val Tyr Asp Met Val Val Arg Gly Asn Cys Phe
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260 265 270

Cys Tyr Gly His Ala Ser Glu Cys Ala Pro Val Asp Gly Phe Asn Glu
275 280 285

Glu Val Glu Gly Met Val His Gly His Cys Met Cys Arg His Asn Thr
290 295 300

Lys Gly Leu Asn Cys Glu Leu Cys Met Asp Phe Tyr His Asp Leu Pro
305 310 315 320

Trp Arg Pro Ala Glu Gly Arg Asn Ser Asn Ala Cys Lys Lys Cys Asn
325 330 335

Cys Asn Glu His Ser Ile Ser Cys His Phe Asp Met Ala Val Tyr Leu
340 345 350

Ala Thr Gly Asn Val Ser Gly Gly Val Cys Asp Asp Cys Gln His Asn
355 360 365

Thr Met Gly Arg Asn Cys Glu Gln Cys Lys Pro Phe Tyr Tyr Gln His
370 375 380

Pro Glu Arg Asp Ile Arg Asp Pro Asn Phe Cys Glu Arg Cys Thr Cys
385 390 395 400

Asp Pro Ala Gly Ser Gln Asn Glu Gly Ile Cys Asp Ser Tyr Thr Asp
405 410 415

Phe Ser Thr Gly Leu Ile Ala Gly Gln Cys Arg Cys Lys Leu Asn Val
420 425 430

Glu Gly Glu His Cys Asp Val Cys Lys Glu Gly Phe Tyr Asp Leu Ser
435 440 445

Ser Glu Asp Pro Phe Gly Cys Lys Ser Cys Ala Cys Asn Pro Leu Gly
450 455 460

Thr Ile Pro Gly Gly Asn Pro Cys Asp Ser Glu Thr Gly His Cys Tyr
465 470 475 480

Cys Lys Arg Leu Val Thr Gly Gln His Cys Asp Gln Cys Leu Pro Glu
485 490 495

His Trp Gly Leu Ser Asn Asp Leu Asp Gly Cys Arg Pro Cys Asp Cys
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Asp Leu Gly Gly Ala Leu Asn Asn Ser Cys Phe Ala Glu Ser Gly Gln
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Cys Ser Cys Arg Pro His Met Ile Gly Arg Gln Cys Asn Glu Val Glu
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Pro Gly Tyr Tyr Phe Ala Thr Leu Asp His Tyr Leu Tyr Glu Ala Glu
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Glu Ala Asn Leu Gly Pro Gly Val Ser Ile Val Glu Arg Gln Tyr Ile
565 570 575

Gln Asp Arg Ile Pro Ser Trp Thr Gly Ala Gly Phe Val Arg Val Pro
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Glu Gly Ala Tyr Leu Glu Phe Phe Ile Asp Asn Ile Pro Tyr Ser Met
595 600 605

Glu Tyr Asp Ile Leu Ile Arg Tyr Glu Pro Gln Leu Pro Asp His Trp
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Glu Lys Ala Val Ile Thr Val Gln Arg Pro Gly Arg Ile Pro Thr Ser
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Ser Arg Cys Gly Asn Thr Ile Pro Asp Asp Asp Asn Gln Val Val Ser
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Leu Ser Pro Gly Ser Arg Tyr Val Val Leu Pro Arg Pro Val Cys Phe
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Glu Lys Gly Thr Asn Tyr Thr Val Arg Leu Glu Leu Pro Gln Tyr Thr
675 680 685

Ser Ser Asp Ser Asp Val Glu Ser Pro Tyr Thr Leu Ile Asp Ser Leu
690 695 700

Val Leu Met Pro Tyr Cys Lys Ser Leu Asp Ile Phe Thr Val Gly Gly
705 710 715 720

Ser Gly Asp Gly Val Val Thr Asn Ser Ala Trp Glu Thr Phe Gln Arg
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Tyr Arg Cys Leu Glu Asn Ser Arg Ser Val Val Lys Thr Pro Met Thr
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Asp Val Cys Arg Asn Ile Ile Phe Ser Ile Ser Ala Leu Leu His Gln
755 760 765

Thr Gly Leu Ala Cys Glu Cys Asp Pro Gln Gly Ser Leu Ser Ser Val
770 775 780

Cys Asp Pro Asn Gly Gly Gln Cys Gln Cys Arg Pro Asn Val Val Gly
785 790 795 800

Arg Thr Cys Asn Arg Cys Ala Pro Gly Thr Phe Gly Phe Gly Pro Ser
805 810 815

Gly Cys Lys Pro Cys Glu Cys His Leu Gln Gly Ser Val Asn Ala Phe
820 825 830

Cys Asn Pro Val Thr Gly Gln Cys His Cys Phe Gln Gly Val Tyr Ala
835 840 845

Arg Gln Cys Asp Arg Cys Leu Pro Gly His Trp Gly Phe Pro Ser Cys
850 855 860

Gln Pro Cys Gln Cys Asn Gly His Ala Asp Asp Cys Asp Pro Val Thr
865 870 875 880

Gly Glu Cys Leu Asn Cys Gln Asp Tyr Thr Met Gly His Asn Cys Glu
885 890 895

Arg Cys Leu Ala Gly Tyr Tyr Gly Asp Pro Ile Ile Gly Ser Gly Asp
900 905 910

His Cys Arg Pro Cys Pro Cys Pro Asp Gly Pro Asp Ser Gly Arg Gln
915 920 925

Phe Ala Arg Ser Cys Tyr Gln Asp Pro Val Thr Leu Gln Leu Ala Cys
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Val Cys Asp Pro Gly Tyr Ile Gly Ser Arg Cys Asp Asp Cys Ala Ser
945 950 955 960

Gly Tyr Phe Gly Asn Pro Ser Glu Val Gly Gly Ser Cys Gln Pro Cys
965 970 975

Gln Cys His Asn Asn Ile Asp Thr Thr Asp Pro Glu Ala Cys Asp Lys
980 985 990

Glu Thr Gly Arg Cys Leu Lys Cys Leu Tyr His Thr Glu Gly Glu His
995 1000 1005

Cys Gln Phe Cys Arg Phe Gly Tyr Tyr Gly Asp Ala Leu Arg Gln Asp
1010 1015 1020

Cys Arg Lys Cys Val Cys Asn Tyr Leu Gly Thr Val Gln Glu His Cys
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Asn Gly Ser Asp Cys Gln Cys Asp Lys Ala Thr Gly Gln Cys Leu Cys
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Leu Pro Asn Val Ile Gly Gln Asn Cys Asp Arg Cys Ala Pro Asn Thr
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Trp Gln Leu Ala Ser Gly Thr Gly Cys Asp Pro Cys Asn Cys Asn Ala
1075 1080 1085

Ala His Ser Phe Gly Pro Ser Cys Asn Glu Phe Thr Gly Gln Cys Gln
1090 1095 1100

Cys Met Pro Gly Phe Gly Gly Arg Thr Cys Ser Glu Cys Gln Glu Leu
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Phe Trp Gly Asp Pro Asp Val Glu Cys Arg Ala Cys Asp Cys Asp Pro
1125 1130 1135

Arg Gly Ile Glu Thr Pro Gln Cys Asp Gln Ser Thr Gly Gln Cys Val
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Cys Val Glu Gly Val Glu Gly Pro Arg Cys Asp Lys Cys Thr Arg Gly
1155 1160 1165

Tyr Ser Gly Val Phe Pro Asp Cys Thr Pro Cys His Gln Cys Phe Ala
1170 1175 1180

Leu Trp Asp Val Ile Ile Ala Glu Leu Thr Asn Arg Thr His Arg Phe
1185 1190 1195 1200

Leu Glu Lys Ala Lys Ala Leu Lys Ile Ser Gly Val Ile Gly Pro Tyr
1205 1210 1215

Arg Glu Thr Val Asp Ser Val Glu Arg Lys Val Ser Glu Ile Lys Asp
1220 1225 1230

Ile L u Ala Gln Ser Pro Ala Ala Glu Pro Leu Lys Asn Ile Gly Asn

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      1235                1240                1245

Leu Phe Glu Glu Ala Glu Lys Leu Ile Lys Asp Val Thr Glu Met Met
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Ala Gln Val Glu Val Lys Leu Ser Asp Thr Thr Ser Gln Ser Asn Ser
1265                1270                1275                1280

Thr Ala Lys Glu Leu Asp Ser Leu Gln Thr Glu Ala Glu Ser Leu Asp
               1285                1290                1295

Asn Thr Val Lys Glu Leu Ala Glu Gln Leu Glu Phe Ile Lys Asn Ser
           1300                1305                1310

Asp Ile Arg Gly Ala Leu Asp Ser Ile Thr Lys Tyr Phe Gln Met Ser
       1315                1320                1325

Leu Glu Ala Glu Glu Arg Val Asn Ala Ser Thr Thr Glu Pro Asn Ser
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Thr Val Glu Gln Ser Ala Leu Met Arg Asp Arg Val Glu Asp Val Met
1345                1350                1355                1360

Met Glu Arg Glu Ser Gln Phe Lys Glu Lys Gln Glu Glu Gln Ala Arg
               1365                1370                1375

Leu Leu Asp Glu Leu Ala Gly Lys Leu Gln Ser Leu Asp Leu Ser Ala
           1380                1385                1390

Ala Ala Glu Met Thr Cys Gly Thr Pro Pro Gly Ala Ser Cys Ser Glu
       1395                1400                1405

Thr Glu Cys Gly Gly Pro Asn Cys Arg Thr Asp Glu Gly Glu Arg Lys
   1410                1415                1420

Cys Gly Gly Pro Gly Cys Gly Gly Leu Val Thr Val Ala His Asn Ala
1425                1430                1435                1440

Trp Gln Lys Ala Met Asp Leu Asp Gln Asp Val Leu Ser Ala Leu Ala
               1445                1450                1455

Glu Val Glu Gln Leu Ser Lys Met Val Ser Glu Ala Lys Leu Arg Ala
           1460                1465                1470

Asp Glu Ala Lys Gln Ser Ala Glu Asp Ile Leu Leu Lys Thr Asn Ala
       1475                1480                1485

Thr Lys Glu Lys Met Asp Lys Ser Asn Glu Glu Leu Arg Asn Leu Ile
   1490                1495                1500

Lys Gln Ile Arg Asn Phe Leu Thr Gln Asp Ser Ala Asp Leu Asp Ser
1505                1510                1515                1520

Ile Glu Ala Val Ala Asn Glu Val Leu Lys Met Glu Met Pro Ser Thr
               1525                1530                1535

Pro Gln Gln Leu Gln Asn Leu Thr Glu Asp Ile Arg Glu Arg Val Glu
           1540                1545                1550

Ser Leu Ser Gln Val Glu Val Ile Leu Gln His Ser Ala Ala Asp Ile
       1555                1560                1565
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Ala Arg Ala Glu Met Leu Leu Glu Glu Ala Lys Arg Ala Ser Lys Ser
   1570                1575                1580

Ala Thr Asp Val Lys Val Thr Ala Asp Met Val Lys Glu Ala Leu Glu
1585                1590                1595                1600

Glu Ala Glu Lys Ala Gln Val Ala Ala Glu Lys Ala Ile Lys Gln Ala
                1605                1610                1615

Asp Glu Asp Ile Gln Gly Thr Gln Asn Leu Leu Thr Ser Ile Glu Ser
           1620                1625                1630

Glu Thr Ala Ala Ser Glu Glu Thr Leu Phe Asn Ala Ser Gln Arg Ile
       1635                1640                1645

Ser Glu Leu Glu Arg Asn Val Glu Glu Leu Lys Arg Lys Ala Ala Gln
   1650                1655                1660

Asn Ser Gly Glu Ala Glu Tyr Ile Glu Lys Val Val Tyr Thr Val Lys
1665                1670                1675                1680

Gln Ser Ala Glu Asp Val Lys Lys Thr Leu Asp Gly Glu Leu Asp Glu
                1685                1690                1695

Lys Tyr Lys Lys Val Glu Asn Leu Ile Ala Lys Lys Thr Glu Glu Ser
           1700                1705                1710

Ala Asp Ala Arg Arg Lys Ala Glu Met Leu Gln Asn Glu Ala Lys Thr
       1715                1720                1725

Leu Leu Ala Gln Ala Asn Ser Lys Leu Gln Leu Leu Lys Asp Leu Glu
   1730                1735                1740

Arg Lys Tyr Glu Asp Asn Gln Arg Tyr Leu Glu Asp Lys Ala Gln Glu
1745                1750                1755                1760

Leu Ala Arg Leu Glu Gly Glu Val Arg Ser Leu Leu Lys Asp Ile Ser
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Gln Lys Val Ala Val Tyr Ser Thr Cys Leu
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Gln Glu Pro Glu Phe Ser Tyr Gly Cys Ala Glu Gly Ser Cys Tyr Pro
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gcc acg ggc gac ctt ctc atc ggc cga gca cag aag ctt tcg gtg acc   96
Ala Thr Gly Asp Leu Leu Ile Gly Arg Ala Gln Lys Leu Ser Val Thr
            20                  25                  30
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tcg acg tgc ggg ctg cac aag ccc gaa ccc tac tgt atc gtc agc cac   144
Ser Thr Cys Gly Leu His Lys Pro Glu Pro Tyr Cys Ile Val Ser His
         35                  40                  45

ttg cag gag gac aaa aaa tgc ttc ata tgc aat tcc caa gat cct tat   192
Leu Gln Glu Asp Lys Lys Cys Phe Ile Cys Asn Ser Gln Asp Pro Tyr
     50                  55                  60

cat gag acc ctg aat cct gac agc cat ctc att gaa aat gtg gtc act   240
His Glu Thr Leu Asn Pro Asp Ser His Leu Ile Glu Asn Val Val Thr
 65                  70                  75                  80

aca ttt gct cca aac cgc ctt aag att tgg tgg caa tct gaa aat ggt   288
Thr Phe Ala Pro Asn Arg Leu Lys Ile Trp Trp Gln Ser Glu Asn Gly
                 85                  90                  95

gtg gaa aat gta act atc caa ctg gat ttg gaa gca gaa ttc cat ttt   336
Val Glu Asn Val Thr Ile Gln Leu Asp Leu Glu Ala Glu Phe His Phe
            100                 105                 110

act cat ctc ata atg act ttc aag aca ttc cgt cca gct gct atg ctg   384
Thr His Leu Ile Met Thr Phe Lys Thr Phe Arg Pro Ala Ala Met Leu
        115                 120                 125

ata gaa cga tcg tcc gac ttt ggg aaa acc tgg ggt gtg tat aga tac   432
Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp Gly Val Tyr Arg Tyr
    130                 135                 140

ttc gcc tat gac tgt gag gcc tcg ttt cca ggc att tca act ggc ccc   480
Phe Ala Tyr Asp Cys Glu Ala Ser Phe Pro Gly Ile Ser Thr Gly Pro
145                 150                 155                 160

atg aaa aaa gtc gat gac ata att tgt gat tct cga tat tct gac att   528
Met Lys Lys Val Asp Asp Ile Ile Cys Asp Ser Arg Tyr Ser Asp Ile
                165                 170                 175

gaa ccc tca act gaa gga gag gtg ata ttt cgt gct tta gat cct gct   576
Glu Pro Ser Thr Glu Gly Glu Val Ile Phe Arg Ala Leu Asp Pro Ala
            180                 185                 190

ttc aaa ata gaa gat cct tat agc cca agg ata cag aat tta tta aaa   624
Phe Lys Ile Glu Asp Pro Tyr Ser Pro Arg Ile Gln Asn Leu Leu Lys
        195                 200                 205

att acc aac ttg aga atc aag ttt gtg aaa ctg cat act ttg gga gat   672
Ile Thr Asn Leu Arg Ile Lys Phe Val Lys Leu His Thr Leu Gly Asp
    210                 215                 220

aac ctt ctg gat tcc agg atg gaa atc aga gaa aag tat tat tat gca   720
Asn Leu Leu Asp Ser Arg Met Glu Ile Arg Glu Lys Tyr Tyr Tyr Ala
225                 230                 235                 240

gtt tat gat atg gtg gtt cga gga aat tgc ttc tgc tat ggt cat gcc   768
Val Tyr Asp Met Val Val Arg Gly Asn Cys Phe Cys Tyr Gly His Ala
                245                 250                 255

agc gaa tgt gcc cct gtg gat gga ttc aat gaa gaa gtg gaa gga atg   816
Ser Glu Cys Ala Pro Val Asp Gly Phe Asn Glu Glu Val Glu Gly Met
            260                 265                 270
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gtt cac gga cac tgc atg tgc agg cat aac acc aag ggc tta aac tgt   864
Val His Gly His Cys Met Cys Arg His Asn Thr Lys Gly Leu Asn Cys
        275                 280                 285

gaa ctc tgc atg gat ttc tac cat gat tta cct tgg aga cct gct gaa   912
Glu Leu Cys Met Asp Phe Tyr His Asp Leu Pro Trp Arg Pro Ala Glu
    290                 295                 300

ggc cga aac agc aac gcc tgt aaa aaa tgt aac tgc aat gaa cat tcc   960
Gly Arg Asn Ser Asn Ala Cys Lys Lys Cys Asn Cys Asn Glu His Ser
305                 310                 315                 320

atc tct tgt cac ttt gac atg gct gtt tac ctg gcc acg ggg aac gtc   1008
Ile Ser Cys His Phe Asp Met Ala Val Tyr Leu Ala Thr Gly Asn Val
                325                 330                 335

agc gga ggc gtg tgt gat gac tgt cag cac aac acc atg ggg cgc aac   1056
Ser Gly Gly Val Cys Asp Asp Cys Gln His Asn Thr Met Gly Arg Asn
            340                 345                 350

tgt gag cag tgc aag ccg ttt tac tac cag cac cca gag agg gac atc   1104
Cys Glu Gln Cys Lys Pro Phe Tyr Tyr Gln His Pro Glu Arg Asp Ile
        355                 360                 365

cga gat cct aat ttc tgt gaa cga tgt acg tgt gac cca gct ggc tct   1152
Arg Asp Pro Asn Phe Cys Glu Arg Cys Thr Cys Asp Pro Ala Gly Ser
    370                 375                 380

caa aat gag gga att tgt gac agc tat act gat ttt tct act ggt ctc   1200
Gln Asn Glu Gly Ile Cys Asp Ser Tyr Thr Asp Phe Ser Thr Gly Leu
385                 390                 395                 400

att gct ggc cag tgt cgg tgt aaa tta aat gtg gaa gga gaa cat tgt   1248
Ile Ala Gly Gln Cys Arg Cys Lys Leu Asn Val Glu Gly Glu His Cys
                405                 410                 415

gat gtt tgc aaa gaa ggc ttc tat gat tta agc agt gaa gat cca ttt   1296
Asp Val Cys Lys Glu Gly Phe Tyr Asp Leu Ser Ser Glu Asp Pro Phe
            420                 425                 430

ggt tgt aaa tct tgt gct tgc aat cct ctg gga aca att cct gga ggg   1344
Gly Cys Lys Ser Cys Ala Cys Asn Pro Leu Gly Thr Ile Pro Gly Gly
        435                 440                 445

aat cct tgt gat tcc gag aca ggt cac tgc tac tgc aag cgt ctg gtg   1392
Asn Pro Cys Asp Ser Glu Thr Gly His Cys Tyr Cys Lys Arg Leu Val
    450                 455                 460

aca gga cag cat tgt gac cag tgc ctg cca gag cac tgg ggc tta agc   1440
Thr Gly Gln His Cys Asp Gln Cys Leu Pro Glu His Trp Gly Leu Ser
465                 470                 475                 480

aat gat ttg gat gga tgt cga cca tgt gac tgt gac ctt ggg gga gcc   1488
Asn Asp Leu Asp Gly Cys Arg Pro Cys Asp Cys Asp Leu Gly Gly Ala
                485                 490                 495

tta aac aac agt tgc ttt gcg gag tca ggc cag tgc tca tgc cgg cct   1536
Leu Asn Asn Ser Cys Phe Ala Glu Ser Gly Gln Cys Ser Cys Arg Pro
            500                 505                 510

cac atg att gga cgt cag tgc aac gaa gtg gaa cct ggt tac tac ttt   1584
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His Met Ile Gly Arg Gln Cys Asn Glu Val Glu Pro Gly Tyr Tyr Phe
        515                 520                 525

gcc acc ctg gat cac tac ctc tat gaa gcg gag gaa gcc aac ttg ggg   1632
Ala Thr Leu Asp His Tyr Leu Tyr Glu Ala Glu Glu Ala Asn Leu Gly
    530                 535                 540

cct ggg gtt agc ata gtg gag cgg caa tat atc cag gac cgg att ccc   1680
Pro Gly Val Ser Ile Val Glu Arg Gln Tyr Ile Gln Asp Arg Ile Pro
545                 550                 555                 560

tcc tgg act gga gcc ggc ttc gtc cga gtg cct gaa ggg gct tat ttg   1728
Ser Trp Thr Gly Ala Gly Phe Val Arg Val Pro Glu Gly Ala Tyr Leu
                565                 570                 575

gag ttt ttc att gac aac ata cca tat tcc atg gag tac gac atc cta   1776
Glu Phe Phe Ile Asp Asn Ile Pro Tyr Ser Met Glu Tyr Asp Ile Leu
            580                 585                 590

att cgc tac gag cca cag cta ccc gac cac tgg gaa aaa gct gtc atc   1824
Ile Arg Tyr Glu Pro Gln Leu Pro Asp His Trp Glu Lys Ala Val Ile
        595                 600                 605

aca gtg cag cga cct gga agg att cca acc agc agc cga tgt ggt aat   1872
Thr Val Gln Arg Pro Gly Arg Ile Pro Thr Ser Ser Arg Cys Gly Asn
    610                 615                 620

acc atc ccc gat gat gac aac cag gtg gtg tca tta tca cca ggc tca   1920
Thr Ile Pro Asp Asp Asp Asn Gln Val Val Ser Leu Ser Pro Gly Ser
625                 630                 635                 640

aga tat gtc gtc ctt cct cgg ccg gtg tgc ttt gag aag gga aca aac   1968
Arg Tyr Val Val Leu Pro Arg Pro Val Cys Phe Glu Lys Gly Thr Asn
                645                 650                 655

tac acg gtg agg ttg gag ctg cct cag tac acc tcc tct gat agc gac   2016
Tyr Thr Val Arg Leu Glu Leu Pro Gln Tyr Thr Ser Ser Asp Ser Asp
            660                 665                 670

gtg gag agc ccc tac acg ctg atc gat tct ctt gtt ctc atg cca tac   2064
Val Glu Ser Pro Tyr Thr Leu Ile Asp Ser Leu Val Leu Met Pro Tyr
        675                 680                 685

tgt aaa tca ctg gac atc ttc acc gtg gga ggt tca gga gat ggg gtg   2112
Cys Lys Ser Leu Asp Ile Phe Thr Val Gly Gly Ser Gly Asp Gly Val
    690                 695                 700

gtc acc aac agt gcc tgg gaa acc ttt cag aga tac cga tgt cta gag   2160
Val Thr Asn Ser Ala Trp Glu Thr Phe Gln Arg Tyr Arg Cys Leu Glu
705                 710                 715                 720

aac agc aga agc gtt gtg aaa aca ccg atg aca gat gtt tgc aga aac   2208
Asn Ser Arg Ser Val Val Lys Thr Pro Met Thr Asp Val Cys Arg Asn
                725                 730                 735

atc atc ttt agc att tct gcc ctg tta cac cag aca ggc ctg gct tgt   2256
Ile Ile Phe Ser Ile Ser Ala Leu Leu His Gln Thr Gly Leu Ala Cys
            740                 745                 750

gaa tgc gac cct cag ggt tcg tta agt tcc gtg tgt gat ccc aac gga   2304
Glu Cys Asp Pro Gln Gly Ser Leu Ser Ser Val Cys Asp Pro Asn Gly
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        755                 760                 765

ggc cag tgc cag tgc cgg ccc aac gtg gtt gga aga acc tgc aac aga   2352
Gly Gln Cys Gln Cys Arg Pro Asn Val Val Gly Arg Thr Cys Asn Arg
    770                 775                 780

tgt gca cct gga act ttt ggc ttt ggc ccc agt gga tgc aaa cct tgt   2400
Cys Ala Pro Gly Thr Phe Gly Phe Gly Pro Ser Gly Cys Lys Pro Cys
785                 790                 795                 800

gag tgc cat ctg caa gga tct gtc aat gcc ttc tgc aat ccc gtc act   2448
Glu Cys His Leu Gln Gly Ser Val Asn Ala Phe Cys Asn Pro Val Thr
                805                 810                 815

ggc cag tgc cac tgt ttc cag gga gtg tat gct cgg cag tgt gat cgg   2496
Gly Gln Cys His Cys Phe Gln Gly Val Tyr Ala Arg Gln Cys Asp Arg
            820                 825                 830

tgc tta cct ggg cac tgg ggc ttt cca agt tgc cag ccc tgc cag tgc   2544
Cys Leu Pro Gly His Trp Gly Phe Pro Ser Cys Gln Pro Cys Gln Cys
        835                 840                 845

aat ggc cac gcc gat gac tgc gac cca gtg act ggg gag tgc ttg aac   2592
Asn Gly His Ala Asp Asp Cys Asp Pro Val Thr Gly Glu Cys Leu Asn
    850                 855                 860

tgc cag gac tac acc atg ggt cat aac tgt gaa agg tgc ttg gct ggt   2640
Cys Gln Asp Tyr Thr Met Gly His Asn Cys Glu Arg Cys Leu Ala Gly
865                 870                 875                 880

tac tat ggc gac ccc atc att ggg tca ggt gat cac tgc cgc cct tgc   2688
Tyr Tyr Gly Asp Pro Ile Ile Gly Ser Gly Asp His Cys Arg Pro Cys
                885                 890                 895

cct tgc cca gat ggt ccc gac agt gga cgc cag ttt gcc agg agc tgc   2736
Pro Cys Pro Asp Gly Pro Asp Ser Gly Arg Gln Phe Ala Arg Ser Cys
            900                 905                 910

tac caa gat cct gtt act tta cag ctt gcc tgt gtt tgt gat cct gga   2784
Tyr Gln Asp Pro Val Thr Leu Gln Leu Ala Cys Val Cys Asp Pro Gly
        915                 920                 925

tac att ggt tcc aga tgt gac gac tgt gcc tca gga tac ttt ggc aat   2832
Tyr Ile Gly Ser Arg Cys Asp Asp Cys Ala Ser Gly Tyr Phe Gly Asn
    930                 935                 940

cca tca gaa gtt ggg ggg tcg tgt cag cct tgc cag tgt cac aac aac   2880
Pro Ser Glu Val Gly Gly Ser Cys Gln Pro Cys Gln Cys His Asn Asn
945                 950                 955                 960

att gac acg aca gac cca gaa gcc tgt gac aag gag act ggg agg tgt   2928
Ile Asp Thr Thr Asp Pro Glu Ala Cys Asp Lys Glu Thr Gly Arg Cys
                965                 970                 975

ctc aag tgc ctg tac cac acg gaa ggg gaa cac tgt cag ttc tgc cgg   2976
Leu Lys Cys Leu Tyr His Thr Glu Gly Glu His Cys Gln Phe Cys Arg
            980                 985                 990

ttt gga tac tat ggt gat gcc ctc cgg cag gac tgt cga aag tgt gtc   3024
Phe Gly Tyr Tyr Gly Asp Ala Leu Arg Gln Asp Cys Arg Lys Cys Val
        995                1000                1005
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tgt aat tac ctg ggc acc gtg caa gag cac tgt aac ggc tct gac tgc   3072
Cys Asn Tyr Leu Gly Thr Val Gln Glu His Cys Asn Gly Ser Asp Cys
   1010                1015                1020

cag tgc gac aaa gcc act ggt cag tgc ttg tgt ctt cct aat gtg atc   3120
Gln Cys Asp Lys Ala Thr Gly Gln Cys Leu Cys Leu Pro Asn Val Ile
1025                1030                1035                1040

ggg cag aac tgt gac cgc tgt gcg ccc aat acc tgg cag ctg gcc agt   3168
Gly Gln Asn Cys Asp Arg Cys Ala Pro Asn Thr Trp Gln Leu Ala Ser
                1045                1050                1055

ggc act ggc tgt gac cca tgc aac tgc aat gct gct cat tcc ttc ggg   3216
Gly Thr Gly Cys Asp Pro Cys Asn Cys Asn Ala Ala His Ser Phe Gly
          1060                1065                1070

cca tct tgc aat gag ttc acg ggg cag tgc cag tgc atg cct ggg ttt   3264
Pro Ser Cys Asn Glu Phe Thr Gly Gln Cys Gln Cys Met Pro Gly Phe
       1075                1080                1085

gga ggc cgc acc tgc agc gag tgc cag gaa ctc ttc tgg gga gac ccc   3312
Gly Gly Arg Thr Cys Ser Glu Cys Gln Glu Leu Phe Trp Gly Asp Pro
   1090                1095                1100

gac gtg gag tgc cga gcc tgt gac tgt gac ccc agg ggc att gag acg   3360
Asp Val Glu Cys Arg Ala Cys Asp Cys Asp Pro Arg Gly Ile Glu Thr
1105                1110                1115                1120

cca cag tgt gac cag tcc acg ggc cag tgt gtc tgc gtt gag ggt gtt   3408
Pro Gln Cys Asp Gln Ser Thr Gly Gln Cys Val Cys Val Glu Gly Val
                1125                1130                1135

gag ggt cca cgc tgt gac aag tgc acg cga ggg tac tcg ggg gtc ttc   3456
Glu Gly Pro Arg Cys Asp Lys Cys Thr Arg Gly Tyr Ser Gly Val Phe
          1140                1145                1150

cct gac tgc aca ccc tgc cac cag tgc ttt gct ctc tgg gat gtg atc   3504
Pro Asp Cys Thr Pro Cys His Gln Cys Phe Ala Leu Trp Asp Val Ile
       1155                1160                1165

att gcc gag ctg acc aac agg aca cac aga ttc ctg gag aaa gcc aag   3552
Ile Ala Glu Leu Thr Asn Arg Thr His Arg Phe Leu Glu Lys Ala Lys
   1170                1175                1180

gcc ttg aag atc agt ggt gtg atc ggg cct tac cgt gag act gtg gac   3600
Ala Leu Lys Ile Ser Gly Val Ile Gly Pro Tyr Arg Glu Thr Val Asp
1185                1190                1195                1200

tcg gtg gag agg aaa gtc agc gag ata aaa gac atc ctg gcg cag agc   3648
Ser Val Glu Arg Lys Val Ser Glu Ile Lys Asp Ile Leu Ala Gln Ser
                1205                1210                1215

ccc gca gca gag cca ctg aaa aac att ggg aat ctc ttt gag gaa gca   3696
Pro Ala Ala Glu Pro Leu Lys Asn Ile Gly Asn Leu Phe Glu Glu Ala
          1220                1225                1230

gag aaa ctg att aaa gat gtt aca gaa atg atg gct caa gta gaa gtg   3744
Glu Lys Leu Ile Lys Asp Val Thr Glu Met Met Ala Gln Val Glu Val
       1235                1240                1245
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aaa cta tct gac aca act tcc caa agc aac agc aca gcc aaa gaa ctg   3792
Lys Leu Ser Asp Thr Thr Ser Gln Ser Asn Ser Thr Ala Lys Glu Leu
  1250                1255                1260

gat tct cta cag aca gaa gcc gaa agc cta gac aac act gtg aaa gaa   3840
Asp Ser Leu Gln Thr Glu Ala Glu Ser Leu Asp Asn Thr Val Lys Glu
1265                1270                1275                1280

ctt gct gaa caa ctg gaa ttt atc aaa aac tca gat att cgg ggt gcc   3888
Leu Ala Glu Gln Leu Glu Phe Ile Lys Asn Ser Asp Ile Arg Gly Ala
               1285                1290                1295

ttg gat agc att acc aag tat ttc cag atg tct ctt gag gca gag gag   3936
Leu Asp Ser Ile Thr Lys Tyr Phe Gln Met Ser Leu Glu Ala Glu Glu
          1300                1305                1310

agg gtg aat gcc tcc acc aca gaa ccc aac agc act gtg gag cag tca   3984
Arg Val Asn Ala Ser Thr Thr Glu Pro Asn Ser Thr Val Glu Gln Ser
       1315                1320                1325

gcc ctc atg aga gac aga gta gaa gac gtg atg atg gag cga gaa tcc   4032
Ala Leu Met Arg Asp Arg Val Glu Asp Val Met Met Glu Arg Glu Ser
  1330                1335                1340

cag ttc aag gaa aaa caa gag gag cag gct cgc ctc ctt gat gaa ctg   4080
Gln Phe Lys Glu Lys Gln Glu Glu Gln Ala Arg Leu Leu Asp Glu Leu
1345                1350                1355                1360

gca ggc aag cta caa agc cta gac ctt tca gcc gct gcc gaa atg acc   4128
Ala Gly Lys Leu Gln Ser Leu Asp Leu Ser Ala Ala Ala Glu Met Thr
               1365                1370                1375

tgt gga aca ccc cca ggg gcc tcc tgt tcc gag act gaa tgt ggc ggg   4176
Cys Gly Thr Pro Pro Gly Ala Ser Cys Ser Glu Thr Glu Cys Gly Gly
          1380                1385                1390

cca aac tgc aga act gac gaa gga gag agg aag tgt ggg ggg cct ggc   4224
Pro Asn Cys Arg Thr Asp Glu Gly Glu Arg Lys Cys Gly Gly Pro Gly
       1395                1400                1405

tgt ggt ggt ctg gtt act gtt gca cac aac gcc tgg cag aaa gcc atg   4272
Cys Gly Gly Leu Val Thr Val Ala His Asn Ala Trp Gln Lys Ala Met
  1410                1415                1420

gac ttg gac caa gat gtc ctg agt gcc ctg gct gaa gtg gaa cag ctc   4320
Asp Leu Asp Gln Asp Val Leu Ser Ala Leu Ala Glu Val Glu Gln Leu
1425                1430                1435                1440

tcc aag atg gtc tct gaa gca aaa ctg agg gca gat gag gca aaa caa   4368
Ser Lys Met Val Ser Glu Ala Lys Leu Arg Ala Asp Glu Ala Lys Gln
               1445                1450                1455

agt gct gaa gac att ctg ttg aag aca aat gct acc aaa gaa aaa atg   4416
Ser Ala Glu Asp Ile Leu Leu Lys Thr Asn Ala Thr Lys Glu Lys Met
          1460                1465                1470

gac aag agc aat gag gag ctg aga aat cta atc aag caa atc aga aac   4464
Asp Lys Ser Asn Glu Glu Leu Arg Asn Leu Ile Lys Gln Ile Arg Asn
       1475                1480                1485

ttt ttg acc cag gat agt gct gat ttg gac agc att gaa gca gtt gct   4512
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Phe Leu Thr Gln Asp Ser Ala Asp Leu Asp Ser Ile Glu Ala Val Ala
   1490                1495                1500

aat gaa gta ttg aaa atg gag atg cct agc acc cca cag cag tta cag   4560
Asn Glu Val Leu Lys Met Glu Met Pro Ser Thr Pro Gln Gln Leu Gln
1505                1510                1515                1520

aac ttg aca gaa gat ata cgt gaa cga gtt gaa agc ctt tct caa gta   4608
Asn Leu Thr Glu Asp Ile Arg Glu Arg Val Glu Ser Leu Ser Gln Val
               1525                1530                1535

gag gtt att ctt cag cat agt gct gct gac att gcc aga gct gag atg   4656
Glu Val Ile Leu Gln His Ser Ala Ala Asp Ile Ala Arg Ala Glu Met
          1540                1545                1550

ttg tta gaa gaa gct aaa aga gca agc aaa agt gca aca gat gtt aaa   4704
Leu Leu Glu Glu Ala Lys Arg Ala Ser Lys Ser Ala Thr Asp Val Lys
       1555                1560                1565

gtc act gca gat atg gta aag gaa gct ctg gaa gaa gca gaa aag gcc   4752
Val Thr Ala Asp Met Val Lys Glu Ala Leu Glu Glu Ala Glu Lys Ala
   1570                1575                1580

cag gtc gca gca gag aag gca att aaa caa gca gat gaa gac att caa   4800
Gln Val Ala Ala Glu Lys Ala Ile Lys Gln Ala Asp Glu Asp Ile Gln
1585                1590                1595                1600

gga acc cag aac ctg tta act tcg att gag tct gaa aca gca gct tct   4848
Gly Thr Gln Asn Leu Leu Thr Ser Ile Glu Ser Glu Thr Ala Ala Ser
               1605                1610                1615

gag gaa acc ttg ttc aac gcg tcc cag cgc atc agc gag tta gag agg   4896
Glu Glu Thr Leu Phe Asn Ala Ser Gln Arg Ile Ser Glu Leu Glu Arg
          1620                1625                1630

aat gtg gaa gaa ctt aag cgg aaa gct gcc caa aac tcc ggg gag gca   4944
Asn Val Glu Glu Leu Lys Arg Lys Ala Ala Gln Asn Ser Gly Glu Ala
       1635                1640                1645

gaa tat att gaa aaa gta gta tat act gtg aag caa agt gca gaa gat   4992
Glu Tyr Ile Glu Lys Val Val Tyr Thr Val Lys Gln Ser Ala Glu Asp
   1650                1655                1660

gtt aag aag act tta gat ggt gaa ctt gat gaa aag tat aaa aaa gta   5040
Val Lys Lys Thr Leu Asp Gly Glu Leu Asp Glu Lys Tyr Lys Lys Val
1665                1670                1675                1680

gaa aat tta att gcc aaa aaa act gaa gag tca gct gat gcc aga agg   5088
Glu Asn Leu Ile Ala Lys Lys Thr Glu Glu Ser Ala Asp Ala Arg Arg
               1685                1690                1695

aaa gcc gaa atg cta caa aat gaa gca aaa act ctt tta gct caa gca   5136
Lys Ala Glu Met Leu Gln Asn Glu Ala Lys Thr Leu Leu Ala Gln Ala
          1700                1705                1710

aat agc aag ctg caa ctg ctc aaa gat tta gaa aga aaa tat gaa gac   5184
Asn Ser Lys Leu Gln Leu Leu Lys Asp Leu Glu Arg Lys Tyr Glu Asp
       1715                1720                1725

aat caa aga tac tta gaa gat aaa gct caa gaa tta gca aga ctg gaa   5232
Asn Gln Arg Tyr Leu Glu Asp Lys Ala Gln Glu Leu Ala Arg Leu Glu
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   1730                1735                1740

gga gaa gtc cgt tca ctc cta aag gat ata agc cag aaa gtt gct gtg   5280
Gly Glu Val Arg Ser Leu Leu Lys Asp Ile Ser Gln Lys Val Ala Val
1745                1750                1755                1760

tat agc aca tgc ttg taacagagga gaataaaaaa tggctgaggt gaacaaggta   5335
Tyr Ser Thr Cys Leu
                1765

aaacaactac attttaaaaa ctgacttaat gctcttcaaa ataaaacatc acctatttaa 5395

tgtttttaat cacattttgt atgagttaaa taaagccc                         5433


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<212> PRT
<213> Homo sapiens

<400> 16
Gln Glu Pro Glu Phe Ser Tyr Gly Cys Ala Glu Gly Ser Cys Tyr Pro
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Ala Thr Gly Asp Leu Leu Ile Gly Arg Ala Gln Lys Leu Ser Val Thr
             20                  25                  30

Ser Thr Cys Gly Leu His Lys Pro Glu Pro Tyr Cys Ile Val Ser His
         35                  40                  45

Leu Gln Glu Asp Lys Lys Cys Phe Ile Cys Asn Ser Gln Asp Pro Tyr
     50                  55                  60

His Glu Thr Leu Asn Pro Asp Ser His Leu Ile Glu Asn Val Val Thr
 65                  70                  75                  80

Thr Phe Ala Pro Asn Arg Leu Lys Ile Trp Trp Gln Ser Glu Asn Gly
                 85                  90                  95

Val Glu Asn Val Thr Ile Gln Leu Asp Leu Glu Ala Glu Phe His Phe
            100                 105                 110

Thr His Leu Ile Met Thr Phe Lys Thr Phe Arg Pro Ala Ala Met Leu
        115                 120                 125

Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp Gly Val Tyr Arg Tyr
    130                 135                 140

Phe Ala Tyr Asp Cys Glu Ala Ser Phe Pro Gly Ile Ser Thr Gly Pro
145                 150                 155                 160

Met Lys Lys Val Asp Asp Ile Ile Cys Asp Ser Arg Tyr Ser Asp Ile
                165                 170                 175

Glu Pro Ser Thr Glu Gly Glu Val Ile Phe Arg Ala Leu Asp Pro Ala
            180                 185                 190

Phe Lys Ile Glu Asp Pro Tyr Ser Pro Arg Ile Gln Asn Leu Leu Lys
        195                 200                 205

Ile Thr Asn Leu Arg Ile Lys Phe Val Lys Leu His Thr Leu Gly Asp
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    210                 215                 220

Asn Leu Leu Asp Ser Arg Met Glu Ile Arg Glu Lys Tyr Tyr Tyr Ala
225                 230                 235                 240

Val Tyr Asp Met Val Val Arg Gly Asn Cys Phe Cys Tyr Gly His Ala
                245                 250                 255

Ser Glu Cys Ala Pro Val Asp Gly Phe Asn Glu Glu Val Glu Gly Met
            260                 265                 270

Val His Gly His Cys Met Cys Arg His Asn Thr Lys Gly Leu Asn Cys
        275                 280                 285

Glu Leu Cys Met Asp Phe Tyr His Asp Leu Pro Trp Arg Pro Ala Glu
    290                 295                 300

Gly Arg Asn Ser Asn Ala Cys Lys Lys Cys Asn Cys Asn Glu His Ser
305                 310                 315                 320

Ile Ser Cys His Phe Asp Met Ala Val Tyr Leu Ala Thr Gly Asn Val
                325                 330                 335

Ser Gly Gly Val Cys Asp Asp Cys Gln His Asn Thr Met Gly Arg Asn
            340                 345                 350

Cys Glu Gln Cys Lys Pro Phe Tyr Tyr Gln His Pro Glu Arg Asp Ile
        355                 360                 365

Arg Asp Pro Asn Phe Cys Glu Arg Cys Thr Cys Asp Pro Ala Gly Ser
    370                 375                 380

Gln Asn Glu Gly Ile Cys Asp Ser Tyr Thr Asp Phe Ser Thr Gly Leu
385                 390                 395                 400

Ile Ala Gly Gln Cys Arg Cys Lys Leu Asn Val Glu Gly Glu His Cys
                405                 410                 415

Asp Val Cys Lys Glu Gly Phe Tyr Asp Leu Ser Ser Glu Asp Pro Phe
            420                 425                 430

Gly Cys Lys Ser Cys Ala Cys Asn Pro Leu Gly Thr Ile Pro Gly Gly
        435                 440                 445

Asn Pro Cys Asp Ser Glu Thr Gly His Cys Tyr Cys Lys Arg Leu Val
    450                 455                 460

Thr Gly Gln His Cys Asp Gln Cys Leu Pro Glu His Trp Gly Leu Ser
465                 470                 475                 480

Asn Asp Leu Asp Gly Cys Arg Pro Cys Asp Cys Asp Leu Gly Gly Ala
                485                 490                 495

Leu Asn Asn Ser Cys Phe Ala Glu Ser Gly Gln Cys Ser Cys Arg Pro
            500                 505                 510

His Met Ile Gly Arg Gln Cys Asn Glu Val Glu Pro Gly Tyr Tyr Phe
        515                 520                 525

Ala Thr Leu Asp His Tyr Leu Tyr Glu Ala Glu Glu Ala Asn Leu Gly
    530                 535                 540
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Pro Gly Val Ser Ile Val Glu Arg Gln Tyr Ile Gln Asp Arg Ile Pro
545                 550                 555                 560

Ser Trp Thr Gly Ala Gly Phe Val Arg Val Pro Glu Gly Ala Tyr Leu
                565                 570                 575

Glu Phe Phe Ile Asp Asn Ile Pro Tyr Ser Met Glu Tyr Asp Ile Leu
            580                 585                 590

Ile Arg Tyr Glu Pro Gln Leu Pro Asp His Trp Glu Lys Ala Val Ile
        595                 600                 605

Thr Val Gln Arg Pro Gly Arg Ile Pro Thr Ser Ser Arg Cys Gly Asn
    610                 615                 620

Thr Ile Pro Asp Asp Asp Asn Gln Val Val Ser Leu Ser Pro Gly Ser
625                 630                 635                 640

Arg Tyr Val Val Leu Pro Arg Pro Val Cys Phe Glu Lys Gly Thr Asn
                645                 650                 655

Tyr Thr Val Arg Leu Glu Leu Pro Gln Tyr Thr Ser Ser Asp Ser Asp
            660                 665                 670

Val Glu Ser Pro Tyr Thr Leu Ile Asp Ser Leu Val Leu Met Pro Tyr
        675                 680                 685

Cys Lys Ser Leu Asp Ile Phe Thr Val Gly Gly Ser Gly Asp Gly Val
    690                 695                 700

Val Thr Asn Ser Ala Trp Glu Thr Phe Gln Arg Tyr Arg Cys Leu Glu
705                 710                 715                 720

Asn Ser Arg Ser Val Val Lys Thr Pro Met Thr Asp Val Cys Arg Asn
                725                 730                 735

Ile Ile Phe Ser Ile Ser Ala Leu Leu His Gln Thr Gly Leu Ala Cys
            740                 745                 750

Glu Cys Asp Pro Gln Gly Ser Leu Ser Ser Val Cys Asp Pro Asn Gly
        755                 760                 765

Gly Gln Cys Gln Cys Arg Pro Asn Val Val Gly Arg Thr Cys Asn Arg
    770                 775                 780

Cys Ala Pro Gly Thr Phe Gly Phe Gly Pro Ser Gly Cys Lys Pro Cys
785                 790                 795                 800

Glu Cys His Leu Gln Gly Ser Val Asn Ala Phe Cys Asn Pro Val Thr
                805                 810                 815

Gly Gln Cys His Cys Phe Gln Gly Val Tyr Ala Arg Gln Cys Asp Arg
            820                 825                 830

Cys Leu Pro Gly His Trp Gly Phe Pro Ser Cys Gln Pro Cys Gln Cys
        835                 840                 845

Asn Gly His Ala Asp Asp Cys Asp Pro Val Thr Gly Glu Cys Leu Asn
    850                 855                 860
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Cys Gln Asp Tyr Thr Met Gly His Asn Cys Glu Arg Cys Leu Ala Gly
865                 870                 875                 880

Tyr Tyr Gly Asp Pro Ile Ile Gly Ser Gly Asp His Cys Arg Pro Cys
                885                 890                 895

Pro Cys Pro Asp Gly Pro Asp Ser Gly Arg Gln Phe Ala Arg Ser Cys
            900                 905                 910

Tyr Gln Asp Pro Val Thr Leu Gln Leu Ala Cys Val Cys Asp Pro Gly
        915                 920                 925

Tyr Ile Gly Ser Arg Cys Asp Asp Cys Ala Ser Gly Tyr Phe Gly Asn
    930                 935                 940

Pro Ser Glu Val Gly Gly Ser Cys Gln Pro Cys Gln Cys His Asn Asn
945                 950                 955                 960

Ile Asp Thr Thr Asp Pro Glu Ala Cys Asp Lys Glu Thr Gly Arg Cys
                965                 970                 975

Leu Lys Cys Leu Tyr His Thr Glu Gly Glu His Cys Gln Phe Cys Arg
            980                 985                 990

Phe Gly Tyr Tyr Gly Asp Ala Leu Arg Gln Asp Cys Arg Lys Cys Val
        995                1000                1005

Cys Asn Tyr Leu Gly Thr Val Gln Glu His Cys Asn Gly Ser Asp Cys
   1010                1015                1020

Gln Cys Asp Lys Ala Thr Gly Gln Cys Leu Cys Leu Pro Asn Val Ile
1025                1030                1035                1040

Gly Gln Asn Cys Asp Arg Cys Ala Pro Asn Thr Trp Gln Leu Ala Ser
                1045                1050                1055

Gly Thr Gly Cys Asp Pro Cys Asn Cys Asn Ala Ala His Ser Phe Gly
            1060                1065                1070

Pro Ser Cys Asn Glu Phe Thr Gly Gln Cys Gln Cys Met Pro Gly Phe
        1075                1080                1085

Gly Gly Arg Thr Cys Ser Glu Cys Gln Glu Leu Phe Trp Gly Asp Pro
   1090                1095                1100

Asp Val Glu Cys Arg Ala Cys Asp Cys Asp Pro Arg Gly Ile Glu Thr
1105                1110                1115                1120

Pro Gln Cys Asp Gln Ser Thr Gly Gln Cys Val Cys Val Glu Gly Val
                1125                1130                1135

Glu Gly Pro Arg Cys Asp Lys Cys Thr Arg Gly Tyr Ser Gly Val Phe
            1140                1145                1150

Pro Asp Cys Thr Pro Cys His Gln Cys Phe Ala Leu Trp Asp Val Ile
        1155                1160                1165

Ile Ala Glu Leu Thr Asn Arg Thr His Arg Phe Leu Glu Lys Ala Lys
   1170                1175                1180

Ala Leu Lys Ile Ser Gly Val Ile Gly Pro Tyr Arg Glu Thr Val Asp
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1185 1190 1195 1200

Ser Val Glu Arg Lys Val Ser Glu Ile Lys Asp Ile Leu Ala Gln Ser
1205 1210 1215

Pro Ala Ala Glu Pro Leu Lys Asn Ile Gly Asn Leu Phe Glu Glu Ala
1220 1225 1230

Glu Lys Leu Ile Lys Asp Val Thr Glu Met Met Ala Gln Val Glu Val
1235 1240 1245

Lys Leu Ser Asp Thr Thr Ser Gln Ser Asn Ser Thr Ala Lys Glu Leu
1250 1255 1260

Asp Ser Leu Gln Thr Glu Ala Glu Ser Leu Asp Asn Thr Val Lys Glu
1265 1270 1275 1280

Leu Ala Glu Gln Leu Glu Phe Ile Lys Asn Ser Asp Ile Arg Gly Ala
1285 1290 1295

Leu Asp Ser Ile Thr Lys Tyr Phe Gln Met Ser Leu Glu Ala Glu Glu
1300 1305 1310

Arg Val Asn Ala Ser Thr Thr Glu Pro Asn Ser Thr Val Glu Gln Ser
1315 1320 1325

Ala Leu Met Arg Asp Arg Val Glu Asp Val Met Met Glu Arg Glu Ser
1330 1335 1340

Gln Phe Lys Glu Lys Gln Glu Glu Gln Ala Arg Leu Leu Asp Glu Leu
1345 1350 1355 1360

Ala Gly Lys Leu Gln Ser Leu Asp Leu Ser Ala Ala Ala Glu Met Thr
1365 1370 1375

Cys Gly Thr Pro Pro Gly Ala Ser Cys Ser Glu Thr Glu Cys Gly Gly
1380 1385 1390

Pro Asn Cys Arg Thr Asp Glu Gly Glu Arg Lys Cys Gly Gly Pro Gly
1395 1400 1405

Cys Gly Gly Leu Val Thr Val Ala His Asn Ala Trp Gln Lys Ala Met
1410 1415 1420

Asp Leu Asp Gln Asp Val Leu Ser Ala Leu Ala Glu Val Glu Gln Leu
1425 1430 1435 1440

Ser Lys Met Val Ser Glu Ala Lys Leu Arg Ala Asp Glu Ala Lys Gln
1445 1450 1455

Ser Ala Glu Asp Ile Leu Leu Lys Thr Asn Ala Thr Lys Glu Lys Met
1460 1465 1470

Asp Lys Ser Asn Glu Glu Leu Arg Asn Leu Ile Lys Gln Ile Arg Asn
1475 1480 1485

Phe Leu Thr Gln Asp Ser Ala Asp Leu Asp Ser Ile Glu Ala Val Ala
1490 1495 1500

Asn Glu Val Leu Lys Met Glu Met Pro Ser Thr Pro Gln Gln Leu Gln
1505 1510 1515 1520

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Asn Leu Thr Glu Asp Ile Arg Glu Arg Val Glu Ser Leu Ser Gln Val
                1525                1530                1535

Glu Val Ile Leu Gln His Ser Ala Ala Asp Ile Ala Arg Ala Glu Met
            1540                1545                1550

Leu Leu Glu Glu Ala Lys Arg Ala Ser Lys Ser Ala Thr Asp Val Lys
        1555                1560                1565

Val Thr Ala Asp Met Val Lys Glu Ala Leu Glu Glu Ala Glu Lys Ala
    1570                1575                1580

Gln Val Ala Ala Glu Lys Ala Ile Lys Gln Ala Asp Glu Asp Ile Gln
1585                1590                1595                1600

Gly Thr Gln Asn Leu Leu Thr Ser Ile Glu Ser Glu Thr Ala Ala Ser
                1605                1610                1615

Glu Glu Thr Leu Phe Asn Ala Ser Gln Arg Ile Ser Glu Leu Glu Arg
            1620                1625                1630

Asn Val Glu Glu Leu Lys Arg Lys Ala Ala Gln Asn Ser Gly Glu Ala
        1635                1640                1645

Glu Tyr Ile Glu Lys Val Val Tyr Thr Val Lys Gln Ser Ala Glu Asp
    1650                1655                1660

Val Lys Lys Thr Leu Asp Gly Glu Leu Asp Glu Lys Tyr Lys Lys Val
1665                1670                1675                1680

Glu Asn Leu Ile Ala Lys Lys Thr Glu Glu Ser Ala Asp Ala Arg Arg
                1685                1690                1695

Lys Ala Glu Met Leu Gln Asn Glu Ala Lys Thr Leu Leu Ala Gln Ala
            1700                1705                1710

Asn Ser Lys Leu Gln Leu Leu Lys Asp Leu Glu Arg Lys Tyr Glu Asp
        1715                1720                1725

Asn Gln Arg Tyr Leu Glu Asp Lys Ala Gln Glu Leu Ala Arg Leu Glu
    1730                1735                1740

Gly Glu Val Arg Ser Leu Leu Lys Asp Ile Ser Gln Lys Val Ala Val
1745                1750                1755                1760

Tyr Ser Thr Cys Leu
                1765


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acatttgcct tttctccccg ctacctctcc agaaaggaag acccgaagaa aagacaggca 120

gcttgcctgc tgcgtcctcc ttcccgtgcc gcgtcccctc gtctgcgagg actggac    177

atg ggg ctg ctc cag gtg ttc gcc ttt ggt gtc cta gcc cta tgg ggc   225
Met Gly Leu Leu Gln Val Phe Ala Phe Gly Val Leu Ala Leu Trp Gly
  1               5                  10                  15

acc cga gtg tgc gct cag gaa ccg gag ttc agc tat ggc tgc gca gaa   273
Thr Arg Val Cys Ala Gln Glu Pro Glu Phe Ser Tyr Gly Cys Ala Glu
             20                  25                  30

ggc agc tgc tac cct gcc act ggc gac ctt ctc atc ggc cga gcg caa   321
Gly Ser Cys Tyr Pro Ala Thr Gly Asp Leu Leu Ile Gly Arg Ala Gln
         35                  40                  45

aag ctc tcc gtg act tcg aca tgt gga ctg cac aaa cca gag ccc tac   369
Lys Leu Ser Val Thr Ser Thr Cys Gly Leu His Lys Pro Glu Pro Tyr
     50                  55                  60

tgt att gtt agc cac ctg cag gag gac aag aaa tgc ttc ata tgt gac   417
Cys Ile Val Ser His Leu Gln Glu Asp Lys Lys Cys Phe Ile Cys Asp
 65                  70                  75                  80

tcc cga gac cct tat cac gag acc ctc aac ccc gac agc cat ctc att   465
Ser Arg Asp Pro Tyr His Glu Thr Leu Asn Pro Asp Ser His Leu Ile
                 85                  90                  95

gag aac gtg gtc acc aca ttt gct cca aac cgc ctt aag atc tgg tgg   513
Glu Asn Val Val Thr Thr Phe Ala Pro Asn Arg Leu Lys Ile Trp Trp
            100                 105                 110

caa tcg gaa aat ggt gtg gag aac gtg acc atc caa ctg gac ctg gaa   561
Gln Ser Glu Asn Gly Val Glu Asn Val Thr Ile Gln Leu Asp Leu Glu
        115                 120                 125

gca gaa ttc cat ttc act cat ctc atc atg acc ttc aag aca ttc cgc   609
Ala Glu Phe His Phe Thr His Leu Ile Met Thr Phe Lys Thr Phe Arg
    130                 135                 140

cca gcc gcc atg ctg atc gag cgg tct tct gac ttt ggg aag act tgg   657
Pro Ala Ala Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp
145                 150                 155                 160

ggc gtg tac aga tac ttc gcc tac gac tgt gag agc tcg ttc cca ggc   705
Gly Val Tyr Arg Tyr Phe Ala Tyr Asp Cys Glu Ser Ser Phe Pro Gly
                165                 170                 175

att tca act gga ccc atg aag aaa gtg gat gac atc atc tgt gac tct   753
Ile Ser Thr Gly Pro Met Lys Lys Val Asp Asp Ile Ile Cys Asp Ser
            180                 185                 190

cga tat tct gac att gag ccc tcg aca gaa gga gag gta ata ttt cgt   801
Arg Tyr Ser Asp Ile Glu Pro Ser Thr Glu Gly Glu Val Ile Phe Arg
        195                 200                 205
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gct tta gat cct gct ttc aaa att gaa gac cct tat agt cca agg ata   849
Ala Leu Asp Pro Ala Phe Lys Ile Glu Asp Pro Tyr Ser Pro Arg Ile
    210                 215                 220

cag aat cta tta aaa atc acc aac ttg aga atc aag ttt gtg aaa ctg   897
Gln Asn Leu Leu Lys Ile Thr Asn Leu Arg Ile Lys Phe Val Lys Leu
225                 230                 235                 240

cac acc ttg ggg gat aac ctt ttg gac tcc aga atg gaa atc cga gag   945
His Thr Leu Gly Asp Asn Leu Leu Asp Ser Arg Met Glu Ile Arg Glu
                245                 250                 255

aag tac tat tac gct gtt tat gat atg gtg gtt cga ggg aac tgc ttc   993
Lys Tyr Tyr Tyr Ala Val Tyr Asp Met Val Val Arg Gly Asn Cys Phe
            260                 265                 270

tgc tat ggc cac gcc agt gaa tgc gcc cct gtg gat gga gtc aat gaa   1041
Cys Tyr Gly His Ala Ser Glu Cys Ala Pro Val Asp Gly Val Asn Glu
        275                 280                 285

gaa gtg gaa gga atg gtt cac ggg cac tgc atg tgc aga cac aac acc   1089
Glu Val Glu Gly Met Val His Gly His Cys Met Cys Arg His Asn Thr
    290                 295                 300

aaa ggc ctg aac tgt gag ctg tgc atg gat ttc tac cac gat ttg ccg   1137
Lys Gly Leu Asn Cys Glu Leu Cys Met Asp Phe Tyr His Asp Leu Pro
305                 310                 315                 320

tgg aga cct gct gaa ggc cgg aac agc aac gcc tgc aaa aaa tgt aac   1185
Trp Arg Pro Ala Glu Gly Arg Asn Ser Asn Ala Cys Lys Lys Cys Asn
                325                 330                 335

tgc aat gaa cat tcc agc tcg tgt cac ttt gac atg gca gtc ttc ctg   1233
Cys Asn Glu His Ser Ser Ser Cys His Phe Asp Met Ala Val Phe Leu
            340                 345                 350

gct act ggc aac gtc agc ggg gga gtg tgt gat aac tgt cag cac aac   1281
Ala Thr Gly Asn Val Ser Gly Gly Val Cys Asp Asn Cys Gln His Asn
        355                 360                 365

acc atg ggg cgc aac tgt gaa cag tgc aaa ccg ttc tac ttc cag cac   1329
Thr Met Gly Arg Asn Cys Glu Gln Cys Lys Pro Phe Tyr Phe Gln His
    370                 375                 380

cct gag agg gac atc cgg gac ccc aat ctc tgt gaa cca tgt acc tgt   1377
Pro Glu Arg Asp Ile Arg Asp Pro Asn Leu Cys Glu Pro Cys Thr Cys
385                 390                 395                 400

gac cca gct ggt tct gag aat ggc ggg atc tgt gat ggg tac act gat   1425
Asp Pro Ala Gly Ser Glu Asn Gly Gly Ile Cys Asp Gly Tyr Thr Asp
                405                 410                 415

ttt tct gtg ggt ctc att gct ggt cag tgt cgg tgc aaa ttg cac gtg   1473
Phe Ser Val Gly Leu Ile Ala Gly Gln Cys Arg Cys Lys Leu His Val
            420                 425                 430

gag gga gag cgc tgt gat gtt tgt aaa gaa ggc ttc tac gac tta agt   1521
Glu Gly Glu Arg Cys Asp Val Cys Lys Glu Gly Phe Tyr Asp Leu Ser
        435                 440                 445

gct gaa gac ccg tat ggt tgt aaa tca tgt gct tgc aat cct ctg gga   1569
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Ala Glu Asp Pro Tyr Gly Cys Lys Ser Cys Ala Cys Asn Pro Leu Gly
    450                 455                 460

aca att cct ggt ggg aat cct tgt gat tct gag act ggc tac tgc tac   1617
Thr Ile Pro Gly Gly Asn Pro Cys Asp Ser Glu Thr Gly Tyr Cys Tyr
465                 470                 475                 480

tgt aag cgc ctg gtg aca gga cag cgc tgt gac cag tgc ctg ccg cag   1665
Cys Lys Arg Leu Val Thr Gly Gln Arg Cys Asp Gln Cys Leu Pro Gln
                485                 490                 495

cac tgg ggt tta agc aat gat ttg gat ggg tgt cga cct tgt gac tgt   1713
His Trp Gly Leu Ser Asn Asp Leu Asp Gly Cys Arg Pro Cys Asp Cys
            500                 505                 510

gac ctt gga ggg gcg ctg aac aat agc tgc tcc gag gac tcc ggc cag   1761
Asp Leu Gly Gly Ala Leu Asn Asn Ser Cys Ser Glu Asp Ser Gly Gln
        515                 520                 525

tgc tcc tgc ctg ccc cac atg att ggg cgg cag tgt aac gag gtg gag   1809
Cys Ser Cys Leu Pro His Met Ile Gly Arg Gln Cys Asn Glu Val Glu
    530                 535                 540

tcc ggt tac tac ttc acc acc ctg gac cac tac atc tac gaa gcc gag   1857
Ser Gly Tyr Tyr Phe Thr Thr Leu Asp His Tyr Ile Tyr Glu Ala Glu
545                 550                 555                 560

gaa gcc aat ctg ggg cct gga gtc gtt gtg gtg gaa agg cag tac att   1905
Glu Ala Asn Leu Gly Pro Gly Val Val Val Val Glu Arg Gln Tyr Ile
                565                 570                 575

cag gac cgc att cct tcc tgg aca gga cct ggc ttc gtc cgg gtg cct   1953
Gln Asp Arg Ile Pro Ser Trp Thr Gly Pro Gly Phe Val Arg Val Pro
            580                 585                 590

gaa ggg gct tat ttg gag ttt ttc att gac aac ata cca tat tcc atg   2001
Glu Gly Ala Tyr Leu Glu Phe Phe Ile Asp Asn Ile Pro Tyr Ser Met
        595                 600                 605

gag tat gaa atc ctg att cgc tat gag cca cag ctg ccg gac cac tgg   2049
Glu Tyr Glu Ile Leu Ile Arg Tyr Glu Pro Gln Leu Pro Asp His Trp
    610                 615                 620

gag aaa gct gtc atc act gta cag cgg ccg ggg aag att cca gcc agc   2097
Glu Lys Ala Val Ile Thr Val Gln Arg Pro Gly Lys Ile Pro Ala Ser
625                 630                 635                 640

agc cga tgt ggt aac acc gtt ccc gat gat gac aac cag gtg gtg tcc   2145
Ser Arg Cys Gly Asn Thr Val Pro Asp Asp Asp Asn Gln Val Val Ser
                645                 650                 655

ttg tca ccg ggc tca aga tac gtt gtc ctc cct cgc ccc gtg tgc ttt   2193
Leu Ser Pro Gly Ser Arg Tyr Val Val Leu Pro Arg Pro Val Cys Phe
            660                 665                 670

gag aag gga atg aac tac acg gtg agg ttg gag ctg ccc cag tat acg   2241
Glu Lys Gly Met Asn Tyr Thr Val Arg Leu Glu Leu Pro Gln Tyr Thr
        675                 680                 685

gca tcg ggc agt gac gtg gag agc cct tac acg ttc atc gac tcg ctt   2289
Ala Ser Gly Ser Asp Val Glu Ser Pro Tyr Thr Phe Ile Asp Ser Leu
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    690                 695                 700

gtt ctc atg ccc tac tgt aaa tcg ctg gac atc ttc act gtt ggc ggc   2337
Val Leu Met Pro Tyr Cys Lys Ser Leu Asp Ile Phe Thr Val Gly Gly
705                 710                 715                 720

tca ggc gat ggg gag gtc acc aat agt gcc tgg gaa acc ttc cag cgc   2385
Ser Gly Asp Gly Glu Val Thr Asn Ser Ala Trp Glu Thr Phe Gln Arg
                725                 730                 735

tac agg tgt ctg gag aac agc agg agt gtg gta aaa aca ccc atg aca   2433
Tyr Arg Cys Leu Glu Asn Ser Arg Ser Val Val Lys Thr Pro Met Thr
            740                 745                 750

gat gtc tgc aga aac att atc ttc agc att tct gcc ttg att cac cag   2481
Asp Val Cys Arg Asn Ile Ile Phe Ser Ile Ser Ala Leu Ile His Gln
        755                 760                 765

acg ggc ctt gct tgt gaa tgt gac ccc cag gga tct ctg agt tct gtg   2529
Thr Gly Leu Ala Cys Glu Cys Asp Pro Gln Gly Ser Leu Ser Ser Val
    770                 775                 780

tgt gac ccc aat ggt ggc cag tgc cag tgc cgt cct aat gtg gtt gga   2577
Cys Asp Pro Asn Gly Gly Gln Cys Gln Cys Arg Pro Asn Val Val Gly
785                 790                 795                 800

aga acc tgc aac agg tgt gcc ccg ggc acc ttt ggc ttt ggc ccc aac   2625
Arg Thr Cys Asn Arg Cys Ala Pro Gly Thr Phe Gly Phe Gly Pro Asn
                805                 810                 815

gga tgc aaa cct tgt gac tgc cat ctg caa ggg tct gcc agt gcc ttc   2673
Gly Cys Lys Pro Cys Asp Cys His Leu Gln Gly Ser Ala Ser Ala Phe
            820                 825                 830

tgc gat gcg atc act ggc cag tgc cac tgt ttc cag ggc atc tat gct   2721
Cys Asp Ala Ile Thr Gly Gln Cys His Cys Phe Gln Gly Ile Tyr Ala
        835                 840                 845

cgg cag tgt gac cga tgt ctc cct ggg tat tgg ggc ttt ccc agc tgc   2769
Arg Gln Cys Asp Arg Cys Leu Pro Gly Tyr Trp Gly Phe Pro Ser Cys
    850                 855                 860

cag ccc tgc cag tgt aat ggt cat gct cta gac tgt gac aca gtg aca   2817
Gln Pro Cys Gln Cys Asn Gly His Ala Leu Asp Cys Asp Thr Val Thr
865                 870                 875                 880

ggg gag tgt ctg agc tgt cag gac tac acc acg ggc cac aac tgc gaa   2865
Gly Glu Cys Leu Ser Cys Gln Asp Tyr Thr Thr Gly His Asn Cys Glu
                885                 890                 895

agg tgc ctg gct ggc tac tac ggt gat ccc atc att ggg tca gga gac   2913
Arg Cys Leu Ala Gly Tyr Tyr Gly Asp Pro Ile Ile Gly Ser Gly Asp
            900                 905                 910

cac tgt cgc cct tgc cct tgt cct gat ggt cct gac agt gga cga cag   2961
His Cys Arg Pro Cys Pro Cys Pro Asp Gly Pro Asp Ser Gly Arg Gln
        915                 920                 925

ttt gcc agg agc tgt tat caa gac ccc gtc act ctc cag ctt gcg tgt   3009
Phe Ala Arg Ser Cys Tyr Gln Asp Pro Val Thr Leu Gln Leu Ala Cys
    930                 935                 940
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gtt tgt gat cct ggg tac att ggc tcc aga tgt gat gac tgt gcc tct   3057
Val Cys Asp Pro Gly Tyr Ile Gly Ser Arg Cys Asp Asp Cys Ala Ser
945                 950                 955                 960

gga ttt ttt ggc aat ccc tca gac ttt ggg ggt tca tgt caa ccg tgt   3105
Gly Phe Phe Gly Asn Pro Ser Asp Phe Gly Gly Ser Cys Gln Pro Cys
                965                 970                 975

cag tgc cac cac aac att gac act acc gat cca gaa gcc tgt gac aag   3153
Gln Cys His His Asn Ile Asp Thr Thr Asp Pro Glu Ala Cys Asp Lys
            980                 985                 990

gac acg gga cga tgc ctc aag tgc ctg tac cac acg gaa ggg gac cat   3201
Asp Thr Gly Arg Cys Leu Lys Cys Leu Tyr His Thr Glu Gly Asp His
        995                1000                1005

tgc cag ctc tgc cag tat ggg tac tac ggc gat gct ctt cgg caa gac   3249
Cys Gln Leu Cys Gln Tyr Gly Tyr Tyr Gly Asp Ala Leu Arg Gln Asp
   1010                1015                1020

tgt aga aag tgt gtc tgc aat tac ctg ggc acg gtg aag gaa cat tgt   3297
Cys Arg Lys Cys Val Cys Asn Tyr Leu Gly Thr Val Lys Glu His Cys
1025                1030                1035                1040

aat ggc tct gac tgc cac tgt gac aaa gcc act ggt cag tgc tcg tgc   3345
Asn Gly Ser Asp Cys His Cys Asp Lys Ala Thr Gly Gln Cys Ser Cys
                1045                1050                1055

ctt ccc aat gtg atc ggg cag aac tgt gac cgg tgt gcg ccc aac acc   3393
Leu Pro Asn Val Ile Gly Gln Asn Cys Asp Arg Cys Ala Pro Asn Thr
           1060                1065                1070

tgg cag ctg gct agc ggg act ggc tgc ggg ccc tgc aat tgc aat gct   3441
Trp Gln Leu Ala Ser Gly Thr Gly Cys Gly Pro Cys Asn Cys Asn Ala
       1075                1080                1085

gcg cat tcc ttt ggg cca tcc tgc aac gag ttc aca ggg cag tgc cag   3489
Ala His Ser Phe Gly Pro Ser Cys Asn Glu Phe Thr Gly Gln Cys Gln
   1090                1095                1100

tgc atg ccg ggc ttt gga ggc cga acc tgc agc gag tgc cag gag ctc   3537
Cys Met Pro Gly Phe Gly Gly Arg Thr Cys Ser Glu Cys Gln Glu Leu
1105                1110                1115                1120

ttc tgg gga gac cct gat gtg gaa tgc cga gcc tgt gac tgt gat ccc   3585
Phe Trp Gly Asp Pro Asp Val Glu Cys Arg Ala Cys Asp Cys Asp Pro
                1125                1130                1135

agg ggc att gag aca cct cag tgt gac cag tcc acg ggc cag tgt gtc   3633
Arg Gly Ile Glu Thr Pro Gln Cys Asp Gln Ser Thr Gly Gln Cys Val
           1140                1145                1150

tgt gtg gag ggt gta gag ggt cct cgc tgc gac aag tgc acc aga ggt   3681
Cys Val Glu Gly Val Glu Gly Pro Arg Cys Asp Lys Cys Thr Arg Gly
       1155                1160                1165

tac tcg ggg gtc ttt cct gac tgc aca ccc tgc cac cag tgc ttt gct   3729
Tyr Ser Gly Val Phe Pro Asp Cys Thr Pro Cys His Gln Cys Phe Ala
   1170                1175                1180
```

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ctc tgg gat gct atc att ggt gag ctg acc aac agg acc cac aaa ttc   3777
Leu Trp Asp Ala Ile Ile Gly Glu Leu Thr Asn Arg Thr His Lys Phe
1185              1190                1195                1200

ctg gag aaa gcc aag gct ctg aaa atc agt ggt gtg att ggt ccc tac   3825
Leu Glu Lys Ala Lys Ala Leu Lys Ile Ser Gly Val Ile Gly Pro Tyr
               1205                1210                1215

cga gag acc gtg gac tct gta gag aag aaa gtc aat gag ata aaa gac   3873
Arg Glu Thr Val Asp Ser Val Glu Lys Lys Val Asn Glu Ile Lys Asp
           1220                1225                1230

atc ctg gcc cag agc cca gca gcg gaa cca ctg aaa aac att ggc att   3921
Ile Leu Ala Gln Ser Pro Ala Ala Glu Pro Leu Lys Asn Ile Gly Ile
       1235                1240                1245

ctc ttc gag gag gca gag aaa cta acc aaa gat gtc aca gaa aag atg   3969
Leu Phe Glu Glu Ala Glu Lys Leu Thr Lys Asp Val Thr Glu Lys Met
   1250                1255                1260

gcg cag gta gaa gtg aaa tta act gat aca gct tca cag agt aac agc   4017
Ala Gln Val Glu Val Lys Leu Thr Asp Thr Ala Ser Gln Ser Asn Ser
1265              1270                1275                1280

aca gct gga gag ctc ggc gca ctg cag gca gaa gca gag agc ctt gac   4065
Thr Ala Gly Glu Leu Gly Ala Leu Gln Ala Glu Ala Glu Ser Leu Asp
               1285                1290                1295

aag acc gtg aag gag ctg gca gaa cag ctg gag ttt atc aaa aac tcc   4113
Lys Thr Val Lys Glu Leu Ala Glu Gln Leu Glu Phe Ile Lys Asn Ser
           1300                1305                1310

gat att cag ggc gcc ttg gat agc atc acc aag tat ttc cag atg tct   4161
Asp Ile Gln Gly Ala Leu Asp Ser Ile Thr Lys Tyr Phe Gln Met Ser
       1315                1320                1325

ctt gag gca gag aag cgg gtg aat gcc tcc acc aca gac ccc aac agc   4209
Leu Glu Ala Glu Lys Arg Val Asn Ala Ser Thr Thr Asp Pro Asn Ser
   1330                1335                1340

act gtg gag cag tct gcc ctc acg cga gac aga gta gaa gat ctg atg   4257
Thr Val Glu Gln Ser Ala Leu Thr Arg Asp Arg Val Glu Asp Leu Met
1345              1350                1355                1360

ttg gag cga gag tct ccg ttc aag gag cag cag gag gaa cag gca cgc   4305
Leu Glu Arg Glu Ser Pro Phe Lys Glu Gln Gln Glu Glu Gln Ala Arg
               1365                1370                1375

ctc ctg gac gaa ctg gcc ggc aaa ctg caa agt ctc gac ctg tcg gct   4353
Leu Leu Asp Glu Leu Ala Gly Lys Leu Gln Ser Leu Asp Leu Ser Ala
           1380                1385                1390

gct gca cag atg acc tgt gga aca cct cca ggg gct gac tgt tct gaa   4401
Ala Ala Gln Met Thr Cys Gly Thr Pro Pro Gly Ala Asp Cys Ser Glu
       1395                1400                1405

agt gaa tgt ggt ggc ccc aac tgc aga act gac gaa gga gag aag aag   4449
Ser Glu Cys Gly Gly Pro Asn Cys Arg Thr Asp Glu Gly Glu Lys Lys
   1410                1415                1420

tgt ggg ggg cct ggc tgt ggt ggt ctg gtc act gtg gcc cac agt gct   4497
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Cys Gly Gly Pro Gly Cys Gly Gly Leu Val Thr Val Ala His Ser Ala
1425                1430                1435                1440

tgg cag aaa gcc atg gat ttt gac cgt gat gtc ctg agt gcc ctg gct   4545
Trp Gln Lys Ala Met Asp Phe Asp Arg Asp Val Leu Ser Ala Leu Ala
                1445                1450                1455

gaa gtc gaa cag ctc tcc aag atg gtc tct gaa gca aaa gtg aga gca   4593
Glu Val Glu Gln Leu Ser Lys Met Val Ser Glu Ala Lys Val Arg Ala
            1460                1465                1470

gat gag gcg aag cag aat gcg cag gat gtc ctg tta aaa aca aat gct   4641
Asp Glu Ala Lys Gln Asn Ala Gln Asp Val Leu Leu Lys Thr Asn Ala
        1475                1480                1485

acc aaa gaa aaa gtg gac aag agc aac gag gac ctg cgg aac ctc atc   4689
Thr Lys Glu Lys Val Asp Lys Ser Asn Glu Asp Leu Arg Asn Leu Ile
    1490                1495                1500

aag cag atc aga aac ttc ctg act gag gat agt gct gat cta gac agt   4737
Lys Gln Ile Arg Asn Phe Leu Thr Glu Asp Ser Ala Asp Leu Asp Ser
1505                1510                1515                1520

att gaa gca gtt gct aat gaa gta ctg aaa agt gga aat gct agc acg   4785
Ile Glu Ala Val Ala Asn Glu Val Leu Lys Ser Gly Asn Ala Ser Thr
                1525                1530                1535

cca cag cag tta cag aac cta aca gaa gac att cgg gag cga gtt gaa   4833
Pro Gln Gln Leu Gln Asn Leu Thr Glu Asp Ile Arg Glu Arg Val Glu
            1540                1545                1550

acc ctc tct caa gta gag gtt att ttg cag cag agt gca gct gac att   4881
Thr Leu Ser Gln Val Glu Val Ile Leu Gln Gln Ser Ala Ala Asp Ile
        1555                1560                1565

gcc aga gct gag ctg ttg ctt gag gaa gct aag aga gca agc aaa agt   4929
Ala Arg Ala Glu Leu Leu Leu Glu Glu Ala Lys Arg Ala Ser Lys Ser
    1570                1575                1580

gca aca gat gtt aaa gtc act gca gac atg gtg aag gaa gca tta gaa   4977
Ala Thr Asp Val Lys Val Thr Ala Asp Met Val Lys Glu Ala Leu Glu
1585                1590                1595                1600

gaa gca gaa aag gcc cag gtt gca gca gag aag gcg att aaa caa gct   5025
Glu Ala Glu Lys Ala Gln Val Ala Ala Glu Lys Ala Ile Lys Gln Ala
                1605                1610                1615

gat gag gat atc caa gga acc caa aac ctg cta aca tcg att gaa tct   5073
Asp Glu Asp Ile Gln Gly Thr Gln Asn Leu Leu Thr Ser Ile Glu Ser
            1620                1625                1630

gaa acg gca gct tct gag gaa acc ctg acc aac gcc tcc cag cgc atc   5121
Glu Thr Ala Ala Ser Glu Glu Thr Leu Thr Asn Ala Ser Gln Arg Ile
        1635                1640                1645

agc aag ctt gag agg aac gtg gaa gag ctt aag cgt aaa gct gcc cag   5169
Ser Lys Leu Glu Arg Asn Val Glu Glu Leu Lys Arg Lys Ala Ala Gln
    1650                1655                1660

aac tct ggg gag gca gaa tat atc gaa aaa gta gta tat tct gta aaa   5217
Asn Ser Gly Glu Ala Glu Tyr Ile Glu Lys Val Val Tyr Ser Val Lys
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1665                1670                1675                1680

cag aat gca gac gat gtt aaa aag act cta gat ggc gaa ctt gat gaa   5265
Gln Asn Ala Asp Asp Val Lys Lys Thr Leu Asp Gly Glu Leu Asp Glu
                1685                1690                1695

aag tat aag aag gta gaa agt tta att gcc caa aaa act gaa gag tca   5313
Lys Tyr Lys Lys Val Glu Ser Leu Ile Ala Gln Lys Thr Glu Glu Ser
            1700                1705                1710

gca gat gcc agg agg aaa gct gag ctg cta caa aat gaa gca aaa aca   5361
Ala Asp Ala Arg Arg Lys Ala Glu Leu Leu Gln Asn Glu Ala Lys Thr
        1715                1720                1725

ctc ttg gct caa gct aac agc aag ctc cag ctg ttg gaa gac tta gaa   5409
Leu Leu Ala Gln Ala Asn Ser Lys Leu Gln Leu Leu Glu Asp Leu Glu
    1730                1735                1740

aga aaa tat gag gac aat caa aaa tac tta gaa gat aaa gct caa gaa   5457
Arg Lys Tyr Glu Asp Asn Gln Lys Tyr Leu Glu Asp Lys Ala Gln Glu
1745                1750                1755                1760

ttg gtg cga ctg gaa gga gag gtt cgc tcc ctc ctt aag gac ata agt   5505
Leu Val Arg Leu Glu Gly Glu Val Arg Ser Leu Leu Lys Asp Ile Ser
                1765                1770                1775

gag aaa gtt gcg gtt tac agc acc tgc tta taacaggaag gggctgtaga     5555
Glu Lys Val Ala Val Tyr Ser Thr Cys Leu
            1780                1785

ggggctcggt gaccaaggta aaccacacgc gcaaaccgag gcagtcatct acaaataacc 5615

catcatctat ttaatgtttt taaccaccta cttttgtatg gagttaaata aaagacattg 5675

gttttgtata aaca                                                  5689


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<211> 1786
<212> PRT
<213> Mus musculus

<400> 18
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  1               5                  10                  15

Thr Arg Val Cys Ala Gln Glu Pro Glu Phe Ser Tyr Gly Cys Ala Glu
             20                  25                  30

Gly Ser Cys Tyr Pro Ala Thr Gly Asp Leu Leu Ile Gly Arg Ala Gln
         35                  40                  45

Lys Leu Ser Val Thr Ser Thr Cys Gly Leu His Lys Pro Glu Pro Tyr
     50                  55                  60

Cys Ile Val Ser His Leu Gln Glu Asp Lys Lys Cys Phe Ile Cys Asp
 65                  70                  75                  80

Ser Arg Asp Pro Tyr His Glu Thr Leu Asn Pro Asp Ser His Leu Ile
                 85                  90                  95
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Glu Asn Val Val Thr Thr Phe Ala Pro Asn Arg Leu Lys Ile Trp Trp
            100                 105                 110

Gln Ser Glu Asn Gly Val Glu Asn Val Thr Ile Gln Leu Asp Leu Glu
        115                 120                 125

Ala Glu Phe His Phe Thr His Leu Ile Met Thr Phe Lys Thr Phe Arg
    130                 135                 140

Pro Ala Ala Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp
145                 150                 155                 160

Gly Val Tyr Arg Tyr Phe Ala Tyr Asp Cys Glu Ser Ser Phe Pro Gly
                165                 170                 175

Ile Ser Thr Gly Pro Met Lys Lys Val Asp Asp Ile Ile Cys Asp Ser
            180                 185                 190

Arg Tyr Ser Asp Ile Glu Pro Ser Thr Glu Gly Glu Val Ile Phe Arg
        195                 200                 205

Ala Leu Asp Pro Ala Phe Lys Ile Glu Asp Pro Tyr Ser Pro Arg Ile
    210                 215                 220

Gln Asn Leu Leu Lys Ile Thr Asn Leu Arg Ile Lys Phe Val Lys Leu
225                 230                 235                 240

His Thr Leu Gly Asp Asn Leu Leu Asp Ser Arg Met Glu Ile Arg Glu
                245                 250                 255

Lys Tyr Tyr Tyr Ala Val Tyr Asp Met Val Val Arg Gly Asn Cys Phe
            260                 265                 270

Cys Tyr Gly His Ala Ser Glu Cys Ala Pro Val Asp Gly Val Asn Glu
        275                 280                 285

Glu Val Glu Gly Met Val His Gly His Cys Met Cys Arg His Asn Thr
    290                 295                 300

Lys Gly Leu Asn Cys Glu Leu Cys Met Asp Phe Tyr His Asp Leu Pro
305                 310                 315                 320

Trp Arg Pro Ala Glu Gly Arg Asn Ser Asn Ala Cys Lys Lys Cys Asn
                325                 330                 335

Cys Asn Glu His Ser Ser Ser Cys His Phe Asp Met Ala Val Phe Leu
            340                 345                 350

Ala Thr Gly Asn Val Ser Gly Gly Val Cys Asp Asn Cys Gln His Asn
        355                 360                 365

Thr Met Gly Arg Asn Cys Glu Gln Cys Lys Pro Phe Tyr Phe Gln His
    370                 375                 380

Pro Glu Arg Asp Ile Arg Asp Pro Asn Leu Cys Glu Pro Cys Thr Cys
385                 390                 395                 400

Asp Pro Ala Gly Ser Glu Asn Gly Gly Ile Cys Asp Gly Tyr Thr Asp
                405                 410                 415

Phe Ser Val Gly Leu Ile Ala Gly Gln Cys Arg Cys Lys Leu His Val
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420 425 430

Glu Gly Glu Arg Cys Asp Val Cys Lys Glu Gly Phe Tyr Asp Leu Ser
435 440 445

Ala Glu Asp Pro Tyr Gly Cys Lys Ser Cys Ala Cys Asn Pro Leu Gly
450 455 460

Thr Ile Pro Gly Gly Asn Pro Cys Asp Ser Glu Thr Gly Tyr Cys Tyr
465 470 475 480

Cys Lys Arg Leu Val Thr Gly Gln Arg Cys Asp Gln Cys Leu Pro Gln
485 490 495

His Trp Gly Leu Ser Asn Asp Leu Asp Gly Cys Arg Pro Cys Asp Cys
500 505 510

Asp Leu Gly Gly Ala Leu Asn Asn Ser Cys Ser Glu Asp Ser Gly Gln
515 520 525

Cys Ser Cys Leu Pro His Met Ile Gly Arg Gln Cys Asn Glu Val Glu
530 535 540

Ser Gly Tyr Tyr Phe Thr Thr Leu Asp His Tyr Ile Tyr Glu Ala Glu
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Glu Ala Asn Leu Gly Pro Gly Val Val Val Val Glu Arg Gln Tyr Ile
565 570 575

Gln Asp Arg Ile Pro Ser Trp Thr Gly Pro Gly Phe Val Arg Val Pro
580 585 590

Glu Gly Ala Tyr Leu Glu Phe Phe Ile Asp Asn Ile Pro Tyr Ser Met
595 600 605

Glu Tyr Glu Ile Leu Ile Arg Tyr Glu Pro Gln Leu Pro Asp His Trp
610 615 620

Glu Lys Ala Val Ile Thr Val Gln Arg Pro Gly Lys Ile Pro Ala Ser
625 630 635 640

Ser Arg Cys Gly Asn Thr Val Pro Asp Asp Asp Asn Gln Val Val Ser
645 650 655

Leu Ser Pro Gly Ser Arg Tyr Val Val Leu Pro Arg Pro Val Cys Phe
660 665 670

Glu Lys Gly Met Asn Tyr Thr Val Arg Leu Glu Leu Pro Gln Tyr Thr
675 680 685

Ala Ser Gly Ser Asp Val Glu Ser Pro Tyr Thr Phe Ile Asp Ser Leu
690 695 700

Val Leu Met Pro Tyr Cys Lys Ser Leu Asp Ile Phe Thr Val Gly Gly
705 710 715 720

Ser Gly Asp Gly Glu Val Thr Asn Ser Ala Trp Glu Thr Phe Gln Arg
725 730 735

Tyr Arg Cys Leu Glu Asn Ser Arg Ser Val Val Lys Thr Pro Met Thr
740 745 750

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Asp Val Cys Arg Asn Ile Ile Phe Ser Ile Ser Ala Leu Ile His Gln
        755                 760                 765

Thr Gly Leu Ala Cys Glu Cys Asp Pro Gln Gly Ser Leu Ser Ser Val
    770                 775                 780

Cys Asp Pro Asn Gly Gly Gln Cys Gln Cys Arg Pro Asn Val Val Gly
785                 790                 795                 800

Arg Thr Cys Asn Arg Cys Ala Pro Gly Thr Phe Gly Phe Gly Pro Asn
                805                 810                 815

Gly Cys Lys Pro Cys Asp Cys His Leu Gln Gly Ser Ala Ser Ala Phe
            820                 825                 830

Cys Asp Ala Ile Thr Gly Gln Cys His Cys Phe Gln Gly Ile Tyr Ala
        835                 840                 845

Arg Gln Cys Asp Arg Cys Leu Pro Gly Tyr Trp Gly Phe Pro Ser Cys
    850                 855                 860

Gln Pro Cys Gln Cys Asn Gly His Ala Leu Asp Cys Asp Thr Val Thr
865                 870                 875                 880

Gly Glu Cys Leu Ser Cys Gln Asp Tyr Thr Thr Gly His Asn Cys Glu
                885                 890                 895

Arg Cys Leu Ala Gly Tyr Tyr Gly Asp Pro Ile Ile Gly Ser Gly Asp
            900                 905                 910

His Cys Arg Pro Cys Pro Cys Pro Asp Gly Pro Asp Ser Gly Arg Gln
        915                 920                 925

Phe Ala Arg Ser Cys Tyr Gln Asp Pro Val Thr Leu Gln Leu Ala Cys
    930                 935                 940

Val Cys Asp Pro Gly Tyr Ile Gly Ser Arg Cys Asp Asp Cys Ala Ser
945                 950                 955                 960

Gly Phe Phe Gly Asn Pro Ser Asp Phe Gly Gly Ser Cys Gln Pro Cys
                965                 970                 975

Gln Cys His His Asn Ile Asp Thr Thr Asp Pro Glu Ala Cys Asp Lys
            980                 985                 990

Asp Thr Gly Arg Cys Leu Lys Cys Leu Tyr His Thr Glu Gly Asp His
        995                1000                1005

Cys Gln Leu Cys Gln Tyr Gly Tyr Tyr Gly Asp Ala Leu Arg Gln Asp
   1010                1015                1020

Cys Arg Lys Cys Val Cys Asn Tyr Leu Gly Thr Val Lys Glu His Cys
1025                1030                1035                1040

Asn Gly Ser Asp Cys His Cys Asp Lys Ala Thr Gly Gln Cys Ser Cys
                1045                1050                1055

Leu Pro Asn Val Ile Gly Gln Asn Cys Asp Arg Cys Ala Pro Asn Thr
            1060                1065                1070
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Trp Gln Leu Ala Ser Gly Thr Gly Cys Gly Pro Cys Asn Cys Asn Ala
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Ala His Ser Phe Gly Pro Ser Cys Asn Glu Phe Thr Gly Gln Cys Gln
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Cys Met Pro Gly Phe Gly Gly Arg Thr Cys Ser Glu Cys Gln Glu Leu
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Phe Trp Gly Asp Pro Asp Val Glu Cys Arg Ala Cys Asp Cys Asp Pro
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Arg Gly Ile Glu Thr Pro Gln Cys Asp Gln Ser Thr Gly Gln Cys Val
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Cys Val Glu Gly Val Glu Gly Pro Arg Cys Asp Lys Cys Thr Arg Gly
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Tyr Ser Gly Val Phe Pro Asp Cys Thr Pro Cys His Gln Cys Phe Ala
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Lys Thr Val Lys Glu Leu Ala Glu Gln Leu Glu Phe Ile Lys Asn Ser
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Asp Ile Gln Gly Ala Leu Asp Ser Ile Thr Lys Tyr Phe Gln Met Ser
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Ala Ala Gln Met Thr Cys Gly Thr Pro Pro Gly Ala Asp Cys Ser Glu

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Ser Glu Cys Gly Gly Pro Asn Cys Arg Thr Asp Glu Gly Glu Lys Lys
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Cys Gly Gly Pro Gly Cys Gly Gly Leu Val Thr Val Ala His Ser Ala
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Trp Gln Lys Ala Met Asp Phe Asp Arg Asp Val Leu Ser Ala Leu Ala
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Glu Val Glu Gln Leu Ser Lys Met Val Ser Glu Ala Lys Val Arg Ala
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Asp Glu Ala Lys Gln Asn Ala Gln Asp Val Leu Leu Lys Thr Asn Ala
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Thr Lys Glu Lys Val Asp Lys Ser Asn Glu Asp Leu Arg Asn Leu Ile
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Lys Gln Ile Arg Asn Phe Leu Thr Glu Asp Ser Ala Asp Leu Asp Ser
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Ile Glu Ala Val Ala Asn Glu Val Leu Lys Ser Gly Asn Ala Ser Thr
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Pro Gln Gln Leu Gln Asn Leu Thr Glu Asp Ile Arg Glu Arg Val Glu
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Glu Thr Ala Ala Ser Glu Glu Thr Leu Thr Asn Ala Ser Gln Arg Ile
1635 1640 1645

Ser Lys Leu Glu Arg Asn Val Glu Glu Leu Lys Arg Lys Ala Ala Gln
1650 1655 1660

Asn Ser Gly Glu Ala Glu Tyr Ile Glu Lys Val Val Tyr Ser Val Lys
1665 1670 1675 1680

Gln Asn Ala Asp Asp Val Lys Lys Thr Leu Asp Gly Glu Leu Asp Glu
1685 1690 1695

Lys Tyr Lys Lys Val Glu Ser Leu Ile Ala Gln Lys Thr Glu Glu Ser
1700 1705 1710

Ala Asp Ala Arg Arg Lys Ala Glu Leu Leu Gln Asn Glu Ala Lys Thr
1715 1720 1725

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Leu Leu Ala Gln Ala Asn Ser Lys Leu Gln Leu Leu Glu Asp Leu Glu
   1730                1735                1740

Arg Lys Tyr Glu Asp Asn Gln Lys Tyr Leu Glu Asp Lys Ala Gln Glu
1745                1750                1755                1760

Leu Val Arg Leu Glu Gly Glu Val Arg Ser Leu Leu Lys Asp Ile Ser
               1765                1770                1775

Glu Lys Val Ala Val Tyr Ser Thr Cys Leu
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Glu Pro Tyr Cys Ile Val Ser His Leu Gln Glu Asp Lys Lys Cys Phe
  1               5                  10                  15

ata tgt gac tcc cga gac cct tat cac gag acc ctc aac ccc gac agc   96
Ile Cys Asp Ser Arg Asp Pro Tyr His Glu Thr Leu Asn Pro Asp Ser
             20                  25                  30

cat ctc att gag aac gtg gtc acc aca ttt gct cca aac cgc ctt aag   144
His Leu Ile Glu Asn Val Val Thr Thr Phe Ala Pro Asn Arg Leu Lys
         35                  40                  45

atc tgg tgg caa tcg gaa aat ggt gtg gag aac gtg acc atc caa ctg   192
Ile Trp Trp Gln Ser Glu Asn Gly Val Glu Asn Val Thr Ile Gln Leu
     50                  55                  60

gac ctg gaa gca gaa ttc cat ttc act cat ctc atc atg acc ttc aag   240
Asp Leu Glu Ala Glu Phe His Phe Thr His Leu Ile Met Thr Phe Lys
 65                  70                  75                  80

aca ttc cgc cca gcc gcc atg ctg atc gag cgg tct tct gac ttt ggg   288
Thr Phe Arg Pro Ala Ala Met Leu Ile Glu Arg Ser Ser Asp Phe Gly
                 85                  90                  95

aag act tgg ggc gtg tac aga tac ttc gcc tac gac tgt gag agc tcg   336
Lys Thr Trp Gly Val Tyr Arg Tyr Phe Ala Tyr Asp Cys Glu Ser Ser
            100                 105                 110

ttc cca ggc att tca act gga ccc atg aag aaa gtg gat gac atc atc   384
Phe Pro Gly Ile Ser Thr Gly Pro Met Lys Lys Val Asp Asp Ile Ile
        115                 120                 125

tgt gac tct cga tat tct gac att gag ccc tcg aca gaa gga gag gta   432
Cys Asp Ser Arg Tyr Ser Asp Ile Glu Pro Ser Thr Glu Gly Glu Val
    130                 135                 140

ata ttt cgt gct tta gat cct gct ttc aaa att gaa gac cct tat agt   480
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Ile Phe Arg Ala Leu Asp Pro Ala Phe Lys Ile Glu Asp Pro Tyr Ser
145                 150                 155                 160

cca agg ata cag aat cta tta aaa atc acc aac ttg aga atc aag ttt   528
Pro Arg Ile Gln Asn Leu Leu Lys Ile Thr Asn Leu Arg Ile Lys Phe
                165                 170                 175

gtg aaa ctg cac acc ttg ggg gat aac ctt ttg gac tcc aga atg gaa   576
Val Lys Leu His Thr Leu Gly Asp Asn Leu Leu Asp Ser Arg Met Glu
            180                 185                 190

atc cga gag aag tac tat tac gct gtt tat gat atg gtg gtt cga ggg   624
Ile Arg Glu Lys Tyr Tyr Tyr Ala Val Tyr Asp Met Val Val Arg Gly
        195                 200                 205

aac tgc ttc tgc tat ggc cac gcc agt gaa tgc gcc cct gtg gat gga   672
Asn Cys Phe Cys Tyr Gly His Ala Ser Glu Cys Ala Pro Val Asp Gly
    210                 215                 220

gtc aat gaa gaa gtg gaa gga atg gtt cac ggg cac tgc atg tgc aga   720
Val Asn Glu Glu Val Glu Gly Met Val His Gly His Cys Met Cys Arg
225                 230                 235                 240

cac aac acc aaa ggc ctg aac tgt gag ctg tgc atg gat ttc tac cac   768
His Asn Thr Lys Gly Leu Asn Cys Glu Leu Cys Met Asp Phe Tyr His
                245                 250                 255

gat ttg ccg tgg aga cct gct gaa ggc cgg aac agc aac gcc tgc aaa   816
Asp Leu Pro Trp Arg Pro Ala Glu Gly Arg Asn Ser Asn Ala Cys Lys
            260                 265                 270

aaa tgt aac tgc aat gaa cat tcc agc tcg tgt cac ttt gac atg gca   864
Lys Cys Asn Cys Asn Glu His Ser Ser Ser Cys His Phe Asp Met Ala
        275                 280                 285

gtc ttc ctg gct act ggc aac gtc agc ggg gga gtg tgt gat aac tgt   912
Val Phe Leu Ala Thr Gly Asn Val Ser Gly Gly Val Cys Asp Asn Cys
    290                 295                 300

cag cac aac acc atg ggg cgc aac tgt gaa cag tgc aaa ccg ttc tac   960
Gln His Asn Thr Met Gly Arg Asn Cys Glu Gln Cys Lys Pro Phe Tyr
305                 310                 315                 320

ttc cag cac cct gag agg gac atc cgg gac ccc aat ctc tgt gaa cca  1008
Phe Gln His Pro Glu Arg Asp Ile Arg Asp Pro Asn Leu Cys Glu Pro
                325                 330                 335

tgt acc tgt gac cca gct ggt tct gag aat ggc ggg atc tgt gat ggg  1056
Cys Thr Cys Asp Pro Ala Gly Ser Glu Asn Gly Gly Ile Cys Asp Gly
            340                 345                 350

tac act gat ttt tct gtg ggt ctc att gct ggt cag tgt cgg tgc aaa  1104
Tyr Thr Asp Phe Ser Val Gly Leu Ile Ala Gly Gln Cys Arg Cys Lys
        355                 360                 365

ttg cac gtg gag gga gag cgc tgt gat gtt tgt aaa gaa ggc ttc tac  1152
Leu His Val Glu Gly Glu Arg Cys Asp Val Cys Lys Glu Gly Phe Tyr
    370                 375                 380

gac tta agt gct gaa gac ccg tat ggt tgt aaa tca tgt gct tgc aat  1200
Asp Leu Ser Ala Glu Asp Pro Tyr Gly Cys Lys Ser Cys Ala Cys Asn
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385                 390                 395                 400

cct ctg gga aca att cct ggt ggg aat cct tgt gat tct gag act ggc   1248
Pro Leu Gly Thr Ile Pro Gly Gly Asn Pro Cys Asp Ser Glu Thr Gly
                405                 410                 415

tac tgc tac tgt aag cgc ctg gtg aca gga cag cgc tgt gac cag tgc   1296
Tyr Cys Tyr Cys Lys Arg Leu Val Thr Gly Gln Arg Cys Asp Gln Cys
            420                 425                 430

ctg ccg cag cac tgg ggt tta agc aat gat ttg gat ggg tgt cga cct   1344
Leu Pro Gln His Trp Gly Leu Ser Asn Asp Leu Asp Gly Cys Arg Pro
        435                 440                 445

tgt gac tgt gac ctt gga ggg gcg ctg aac aat agc tgc tcc gag gac   1392
Cys Asp Cys Asp Leu Gly Gly Ala Leu Asn Asn Ser Cys Ser Glu Asp
    450                 455                 460

tcc ggc cag tgc tcc tgc ctg ccc cac atg att ggg cgg cag tgt aac   1440
Ser Gly Gln Cys Ser Cys Leu Pro His Met Ile Gly Arg Gln Cys Asn
465                 470                 475                 480

gag gtg gag tcc ggt tac tac ttc acc acc ctg gac cac tac atc tac   1488
Glu Val Glu Ser Gly Tyr Tyr Phe Thr Thr Leu Asp His Tyr Ile Tyr
                485                 490                 495

gaa gcc gag gaa gcc aat ctg ggg cct gga gtc gtt gtg gtg gaa agg   1536
Glu Ala Glu Glu Ala Asn Leu Gly Pro Gly Val Val Val Val Glu Arg
            500                 505                 510

cag tac att cag gac cgc att cct tcc tgg aca gga cct ggc ttc gtc   1584
Gln Tyr Ile Gln Asp Arg Ile Pro Ser Trp Thr Gly Pro Gly Phe Val
        515                 520                 525

cgg gtg cct gaa ggg gct tat ttg gag ttt ttc att gac aac ata cca   1632
Arg Val Pro Glu Gly Ala Tyr Leu Glu Phe Phe Ile Asp Asn Ile Pro
    530                 535                 540

tat tcc atg gag tat gaa atc ctg att cgc tat gag cca cag ctg ccg   1680
Tyr Ser Met Glu Tyr Glu Ile Leu Ile Arg Tyr Glu Pro Gln Leu Pro
545                 550                 555                 560

gac cac tgg gag aaa gct gtc atc act gta cag cgg ccg ggg aag att   1728
Asp His Trp Glu Lys Ala Val Ile Thr Val Gln Arg Pro Gly Lys Ile
                565                 570                 575

cca gcc agc agc cga tgt ggt aac acc gtt ccc gat gat gac aac cag   1776
Pro Ala Ser Ser Arg Cys Gly Asn Thr Val Pro Asp Asp Asp Asn Gln
            580                 585                 590

gtg gtg tcc ttg tca ccg ggc tca aga tac gtt gtc ctc cct cgc ccc   1824
Val Val Ser Leu Ser Pro Gly Ser Arg Tyr Val Val Leu Pro Arg Pro
        595                 600                 605

gtg tgc ttt gag aag gga atg aac tac acg gtg agg ttg gag ctg ccc   1872
Val Cys Phe Glu Lys Gly Met Asn Tyr Thr Val Arg Leu Glu Leu Pro
    610                 615                 620

cag tat acg gca tcg ggc agt gac gtg gag agc cct tac acg ttc atc   1920
Gln Tyr Thr Ala Ser Gly Ser Asp Val Glu Ser Pro Tyr Thr Phe Ile
625                 630                 635                 640
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gac tcg ctt gtt ctc atg ccc tac tgt aaa tcg ctg gac atc ttc act   1968
Asp Ser Leu Val Leu Met Pro Tyr Cys Lys Ser Leu Asp Ile Phe Thr
                645                 650                 655

gtt ggc ggc tca ggc gat ggg gag gtc acc aat agt gcc tgg gaa acc   2016
Val Gly Gly Ser Gly Asp Gly Glu Val Thr Asn Ser Ala Trp Glu Thr
            660                 665                 670

ttc cag cgc tac agg tgt ctg gag aac agc agg agt gtg gta aaa aca   2064
Phe Gln Arg Tyr Arg Cys Leu Glu Asn Ser Arg Ser Val Val Lys Thr
        675                 680                 685

ccc atg aca gat gtc tgc aga aac att atc ttc agc att tct gcc ttg   2112
Pro Met Thr Asp Val Cys Arg Asn Ile Ile Phe Ser Ile Ser Ala Leu
    690                 695                 700

att cac cag acg ggc ctt gct tgt gaa tgt gac ccc cag gga tct ctg   2160
Ile His Gln Thr Gly Leu Ala Cys Glu Cys Asp Pro Gln Gly Ser Leu
705                 710                 715                 720

agt tct gtg tgt gac ccc aat ggt ggc cag tgc cag tgc cgt cct aat   2208
Ser Ser Val Cys Asp Pro Asn Gly Gly Gln Cys Gln Cys Arg Pro Asn
                725                 730                 735

gtg gtt gga aga acc tgc aac agg tgt gcc ccg ggc acc ttt ggc ttt   2256
Val Val Gly Arg Thr Cys Asn Arg Cys Ala Pro Gly Thr Phe Gly Phe
            740                 745                 750

ggc ccc aac gga tgc aaa cct tgt gac tgc cat ctg caa ggg tct gcc   2304
Gly Pro Asn Gly Cys Lys Pro Cys Asp Cys His Leu Gln Gly Ser Ala
        755                 760                 765

agt gcc ttc tgc gat gcg atc act ggc cag tgc cac tgt ttc cag ggc   2352
Ser Ala Phe Cys Asp Ala Ile Thr Gly Gln Cys His Cys Phe Gln Gly
    770                 775                 780

atc tat gct cgg cag tgt gac cga tgt ctc cct ggg tat tgg ggc ttt   2400
Ile Tyr Ala Arg Gln Cys Asp Arg Cys Leu Pro Gly Tyr Trp Gly Phe
785                 790                 795                 800

ccc agc tgc cag ccc tgc cag tgt aat ggt cat gct cta gac tgt gac   2448
Pro Ser Cys Gln Pro Cys Gln Cys Asn Gly His Ala Leu Asp Cys Asp
                805                 810                 815

aca gtg aca ggg gag tgt ctg agc tgt cag gac tac acc acg ggc cac   2496
Thr Val Thr Gly Glu Cys Leu Ser Cys Gln Asp Tyr Thr Thr Gly His
            820                 825                 830

aac tgc gaa agg tgc ctg gct ggc tac tac ggt gat ccc atc att ggg   2544
Asn Cys Glu Arg Cys Leu Ala Gly Tyr Tyr Gly Asp Pro Ile Ile Gly
        835                 840                 845

tca gga gac cac tgt cgc cct tgc cct tgt cct gat ggt cct gac agt   2592
Ser Gly Asp His Cys Arg Pro Cys Pro Cys Pro Asp Gly Pro Asp Ser
    850                 855                 860

gga cga cag ttt gcc agg agc tgt tat caa gac ccc gtc act ctc cag   2640
Gly Arg Gln Phe Ala Arg Ser Cys Tyr Gln Asp Pro Val Thr Leu Gln
865                 870                 875                 880
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ctt gcg tgt gtt tgt gat cct ggg tac att ggc tcc aga tgt gat gac   2688
Leu Ala Cys Val Cys Asp Pro Gly Tyr Ile Gly Ser Arg Cys Asp Asp
                885                 890                 895

tgt gcc tct gga ttt ttt ggc aat ccc tca gac ttt ggg ggt tca tgt   2736
Cys Ala Ser Gly Phe Phe Gly Asn Pro Ser Asp Phe Gly Gly Ser Cys
            900                 905                 910

caa ccg tgt cag tgc cac cac aac att gac act acc gat cca gaa gcc   2784
Gln Pro Cys Gln Cys His His Asn Ile Asp Thr Thr Asp Pro Glu Ala
        915                 920                 925

tgt gac aag gac acg gga cga tgc ctc aag tgc ctg tac cac acg gaa   2832
Cys Asp Lys Asp Thr Gly Arg Cys Leu Lys Cys Leu Tyr His Thr Glu
    930                 935                 940

ggg gac cat tgc cag ctc tgc cag tat ggg tac tac ggc gat gct ctt   2880
Gly Asp His Cys Gln Leu Cys Gln Tyr Gly Tyr Tyr Gly Asp Ala Leu
945                 950                 955                 960

cgg caa gac tgt aga aag tgt gtc tgc aat tac ctg ggc acg gtg aag   2928
Arg Gln Asp Cys Arg Lys Cys Val Cys Asn Tyr Leu Gly Thr Val Lys
                965                 970                 975

gaa cat tgt aat ggc tct gac tgc cac tgt gac aaa gcc act ggt cag   2976
Glu His Cys Asn Gly Ser Asp Cys His Cys Asp Lys Ala Thr Gly Gln
            980                 985                 990

tgc tcg tgc ctt ccc aat gtg atc ggg cag aac tgt gac cgg tgt gcg   3024
Cys Ser Cys Leu Pro Asn Val Ile Gly Gln Asn Cys Asp Arg Cys Ala
        995                1000                1005

ccc aac acc tgg cag ctg gct agc ggg act ggc tgc ggg ccc tgc aat   3072
Pro Asn Thr Trp Gln Leu Ala Ser Gly Thr Gly Cys Gly Pro Cys Asn
   1010                1015                1020

tgc aat gct gcg cat tcc ttt ggg cca tcc tgc aac gag ttc aca ggg   3120
Cys Asn Ala Ala His Ser Phe Gly Pro Ser Cys Asn Glu Phe Thr Gly
1025                1030                1035                1040

cag tgc cag tgc atg ccg ggc ttt gga ggc cga acc tgc agc gag tgc   3168
Gln Cys Gln Cys Met Pro Gly Phe Gly Gly Arg Thr Cys Ser Glu Cys
                1045                1050                1055

cag gag ctc ttc tgg gga gac cct gat gtg gaa tgc cga gcc tgt gac   3216
Gln Glu Leu Phe Trp Gly Asp Pro Asp Val Glu Cys Arg Ala Cys Asp
            1060                1065                1070

tgt gat ccc agg ggc att gag aca cct cag tgt gac cag tcc acg ggc   3264
Cys Asp Pro Arg Gly Ile Glu Thr Pro Gln Cys Asp Gln Ser Thr Gly
        1075                1080                1085

cag tgt gtc tgt gtg gag ggt gta gag ggt cct cgc tgc gac aag tgc   3312
Gln Cys Val Cys Val Glu Gly Val Glu Gly Pro Arg Cys Asp Lys Cys
   1090                1095                1100

acc aga ggt tac tcg ggg gtc ttt cct gac tgc aca ccc tgc cac cag   3360
Thr Arg Gly Tyr Ser Gly Val Phe Pro Asp Cys Thr Pro Cys His Gln
1105                1110                1115                1120

tgc ttt gct ctc tgg gat gct atc att ggt gag ctg acc aac agg acc   3408
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Cys Phe Ala Leu Trp Asp Ala Ile Ile Gly Glu Leu Thr Asn Arg Thr
                1125                1130                1135

cac aaa ttc ctg gag aaa gcc aag gct ctg aaa atc agt ggt gtg att   3456
His Lys Phe Leu Glu Lys Ala Lys Ala Leu Lys Ile Ser Gly Val Ile
          1140                1145                1150

ggt ccc tac cga gag acc gtg gac tct gta gag aag aaa gtc aat gag   3504
Gly Pro Tyr Arg Glu Thr Val Asp Ser Val Glu Lys Lys Val Asn Glu
       1155                1160                1165

ata aaa gac atc ctg gcc cag agc cca gca gcg gaa cca ctg aaa aac   3552
Ile Lys Asp Ile Leu Ala Gln Ser Pro Ala Ala Glu Pro Leu Lys Asn
   1170                1175                1180

att ggc att ctc ttc gag gag gca gag aaa cta acc aaa gat gtc aca   3600
Ile Gly Ile Leu Phe Glu Glu Ala Glu Lys Leu Thr Lys Asp Val Thr
1185                1190                1195                1200

gaa aag atg gcg cag gta gaa gtg aaa tta act gat aca gct tca cag   3648
Glu Lys Met Ala Gln Val Glu Val Lys Leu Thr Asp Thr Ala Ser Gln
                1205                1210                1215

agt aac agc aca gct gga gag ctc ggc gca ctg cag gca gaa gca gag   3696
Ser Asn Ser Thr Ala Gly Glu Leu Gly Ala Leu Gln Ala Glu Ala Glu
          1220                1225                1230

agc ctt gac aag acc gtg aag gag ctg gca gaa cag ctg gag ttt atc   3744
Ser Leu Asp Lys Thr Val Lys Glu Leu Ala Glu Gln Leu Glu Phe Ile
       1235                1240                1245

aaa aac tcc gat att cag ggc gcc ttg gat agc atc acc aag tat ttc   3792
Lys Asn Ser Asp Ile Gln Gly Ala Leu Asp Ser Ile Thr Lys Tyr Phe
   1250                1255                1260

cag atg tct ctt gag gca gag aag cgg gtg aat gcc tcc acc aca gac   3840
Gln Met Ser Leu Glu Ala Glu Lys Arg Val Asn Ala Ser Thr Thr Asp
1265                1270                1275                1280

ccc aac agc act gtg gag cag tct gcc ctc acg cga gac aga gta gaa   3888
Pro Asn Ser Thr Val Glu Gln Ser Ala Leu Thr Arg Asp Arg Val Glu
                1285                1290                1295

gat ctg atg ttg gag cga gag tct ccg ttc aag gag cag cag gag gaa   3936
Asp Leu Met Leu Glu Arg Glu Ser Pro Phe Lys Glu Gln Gln Glu Glu
          1300                1305                1310

cag gca cgc ctc ctg gac gaa ctg gcc ggc aaa ctg caa agt ctc gac   3984
Gln Ala Arg Leu Leu Asp Glu Leu Ala Gly Lys Leu Gln Ser Leu Asp
       1315                1320                1325

ctg tcg gct gct gca cag atg acc tgt gga aca cct cca ggg gct gac   4032
Leu Ser Ala Ala Ala Gln Met Thr Cys Gly Thr Pro Pro Gly Ala Asp
   1330                1335                1340

tgt tct gaa agt gaa tgt ggt ggc ccc aac tgc aga act gac gaa gga   4080
Cys Ser Glu Ser Glu Cys Gly Gly Pro Asn Cys Arg Thr Asp Glu Gly
1345                1350                1355                1360

gag aag aag tgt ggg ggg cct ggc tgt ggt ggt ctg gtc act gtg gcc   4128
Glu Lys Lys Cys Gly Gly Pro Gly Cys Gly Gly Leu Val Thr Val Ala
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                1365                1370                1375

cac agt gct tgg cag aaa gcc atg gat ttt gac cgt gat gtc ctg agt   4176
His Ser Ala Trp Gln Lys Ala Met Asp Phe Asp Arg Asp Val Leu Ser
          1380                1385                1390

gcc ctg gct gaa gtc gaa cag ctc tcc aag atg gtc tct gaa gca aaa   4224
Ala Leu Ala Glu Val Glu Gln Leu Ser Lys Met Val Ser Glu Ala Lys
       1395                1400                1405

gtg aga gca gat gag gcg aag cag aat gcg cag gat gtc ctg tta aaa   4272
Val Arg Ala Asp Glu Ala Lys Gln Asn Ala Gln Asp Val Leu Leu Lys
   1410                1415                1420

aca aat gct acc aaa gaa aaa gtg gac aag agc aac gag gac ctg cgg   4320
Thr Asn Ala Thr Lys Glu Lys Val Asp Lys Ser Asn Glu Asp Leu Arg
1425                1430                1435                1440

aac ctc atc aag cag atc aga aac ttc ctg act gag gat agt gct gat   4368
Asn Leu Ile Lys Gln Ile Arg Asn Phe Leu Thr Glu Asp Ser Ala Asp
               1445                1450                1455

cta gac agt att gaa gca gtt gct aat gaa gta ctg aaa agt gga aat   4416
Leu Asp Ser Ile Glu Ala Val Ala Asn Glu Val Leu Lys Ser Gly Asn
          1460                1465                1470

gct agc acg cca cag cag tta cag aac cta aca gaa gac att cgg gag   4464
Ala Ser Thr Pro Gln Gln Leu Gln Asn Leu Thr Glu Asp Ile Arg Glu
       1475                1480                1485

cga gtt gaa acc ctc tct caa gta gag gtt att ttg cag cag agt gca   4512
Arg Val Glu Thr Leu Ser Gln Val Glu Val Ile Leu Gln Gln Ser Ala
   1490                1495                1500

gct gac att gcc aga gct gag ctg ttg ctt gag gaa gct aag aga gca   4560
Ala Asp Ile Ala Arg Ala Glu Leu Leu Leu Glu Glu Ala Lys Arg Ala
1505                1510                1515                1520

agc aaa agt gca aca gat gtt aaa gtc act gca gac atg gtg aag gaa   4608
Ser Lys Ser Ala Thr Asp Val Lys Val Thr Ala Asp Met Val Lys Glu
               1525                1530                1535

gca tta gaa gaa gca gaa aag gcc cag gtt gca gca gag aag gcg att   4656
Ala Leu Glu Glu Ala Glu Lys Ala Gln Val Ala Ala Glu Lys Ala Ile
          1540                1545                1550

aaa caa gct gat gag gat atc caa gga acc caa aac ctg cta aca tcg   4704
Lys Gln Ala Asp Glu Asp Ile Gln Gly Thr Gln Asn Leu Leu Thr Ser
       1555                1560                1565

att gaa tct gaa acg gca gct tct gag gaa acc ctg acc aac gcc tcc   4752
Ile Glu Ser Glu Thr Ala Ala Ser Glu Glu Thr Leu Thr Asn Ala Ser
   1570                1575                1580

cag cgc atc agc aag ctt gag agg aac gtg gaa gag ctt aag cgt aaa   4800
Gln Arg Ile Ser Lys Leu Glu Arg Asn Val Glu Glu Leu Lys Arg Lys
1585                1590                1595                1600

gct gcc cag aac tct ggg gag gca gaa tat atc gaa aaa gta gta tat   4848
Ala Ala Gln Asn Ser Gly Glu Ala Glu Tyr Ile Glu Lys Val Val Tyr
               1605                1610                1615
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tct gta aaa cag aat gca gac gat gtt aaa aag act cta gat ggc gaa   4896
Ser Val Lys Gln Asn Ala Asp Asp Val Lys Lys Thr Leu Asp Gly Glu
          1620                1625                1630

ctt gat gaa aag tat aag aag gta gaa agt tta att gcc caa aaa act   4944
Leu Asp Glu Lys Tyr Lys Lys Val Glu Ser Leu Ile Ala Gln Lys Thr
       1635                1640                1645

gaa gag tca gca gat gcc agg agg aaa gct gag ctg cta caa aat gaa   4992
Glu Glu Ser Ala Asp Ala Arg Arg Lys Ala Glu Leu Leu Gln Asn Glu
   1650                1655                1660

gca aaa aca ctc ttg gct caa gct aac agc aag ctc cag ctg ttg gaa   5040
Ala Lys Thr Leu Leu Ala Gln Ala Asn Ser Lys Leu Gln Leu Leu Glu
1665                1670                1675                1680

gac tta gaa aga aaa tat gag gac aat caa aaa tac tta gaa gat aaa   5088
Asp Leu Glu Arg Lys Tyr Glu Asp Asn Gln Lys Tyr Leu Glu Asp Lys
               1685                1690                1695

gct caa gaa ttg gtg cga ctg gaa gga gag gtt cgc tcc ctc ctt aag   5136
Ala Gln Glu Leu Val Arg Leu Glu Gly Glu Val Arg Ser Leu Leu Lys
          1700                1705                1710

gac ata agt gag aaa gtt gcg gtt tac agc acc tgc tta taacaggaag    5185
Asp Ile Ser Glu Lys Val Ala Val Tyr Ser Thr Cys Leu
       1715                1720                1725

gggctgtaga ggggctcggt gaccaaggta aaccacacgc gcaaaccgag gcagtcatct 5245

acaaataacc catcatctat ttaatgtttt taaccaccta cttttgtatg gagttaaata 5305

aaagacattg gttttgtata aaca                                       5329
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Glu Pro Tyr Cys Ile Val Ser His Leu Gln Glu Asp Lys Lys Cys Phe
  1               5                  10                  15

Ile Cys Asp Ser Arg Asp Pro Tyr His Glu Thr Leu Asn Pro Asp Ser
             20                  25                  30

His Leu Ile Glu Asn Val Val Thr Thr Phe Ala Pro Asn Arg Leu Lys
         35                  40                  45

Ile Trp Trp Gln Ser Glu Asn Gly Val Glu Asn Val Thr Ile Gln Leu
     50                  55                  60

Asp Leu Glu Ala Glu Phe His Phe Thr His Leu Ile Met Thr Phe Lys
 65                  70                  75                  80

Thr Phe Arg Pro Ala Ala Met Leu Ile Glu Arg Ser Ser Asp Phe Gly
                 85                  90                  95

Lys Thr Trp Gly Val Tyr Arg Tyr Phe Ala Tyr Asp Cys Glu Ser Ser
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           100                 105                 110

Phe Pro Gly Ile Ser Thr Gly Pro Met Lys Lys Val Asp Asp Ile Ile
        115                 120                 125

Cys Asp Ser Arg Tyr Ser Asp Ile Glu Pro Ser Thr Glu Gly Glu Val
    130                 135                 140

Ile Phe Arg Ala Leu Asp Pro Ala Phe Lys Ile Glu Asp Pro Tyr Ser
145                 150                 155                 160

Pro Arg Ile Gln Asn Leu Leu Lys Ile Thr Asn Leu Arg Ile Lys Phe
                165                 170                 175

Val Lys Leu His Thr Leu Gly Asp Asn Leu Leu Asp Ser Arg Met Glu
            180                 185                 190

Ile Arg Glu Lys Tyr Tyr Tyr Ala Val Tyr Asp Met Val Val Arg Gly
        195                 200                 205

Asn Cys Phe Cys Tyr Gly His Ala Ser Glu Cys Ala Pro Val Asp Gly
    210                 215                 220

Val Asn Glu Glu Val Glu Gly Met Val His Gly His Cys Met Cys Arg
225                 230                 235                 240

His Asn Thr Lys Gly Leu Asn Cys Glu Leu Cys Met Asp Phe Tyr His
                245                 250                 255

Asp Leu Pro Trp Arg Pro Ala Glu Gly Arg Asn Ser Asn Ala Cys Lys
            260                 265                 270

Lys Cys Asn Cys Asn Glu His Ser Ser Ser Cys His Phe Asp Met Ala
        275                 280                 285

Val Phe Leu Ala Thr Gly Asn Val Ser Gly Gly Val Cys Asp Asn Cys
    290                 295                 300

Gln His Asn Thr Met Gly Arg Asn Cys Glu Gln Cys Lys Pro Phe Tyr
305                 310                 315                 320

Phe Gln His Pro Glu Arg Asp Ile Arg Asp Pro Asn Leu Cys Glu Pro
                325                 330                 335

Cys Thr Cys Asp Pro Ala Gly Ser Glu Asn Gly Gly Ile Cys Asp Gly
            340                 345                 350

Tyr Thr Asp Phe Ser Val Gly Leu Ile Ala Gly Gln Cys Arg Cys Lys
        355                 360                 365

Leu His Val Glu Gly Glu Arg Cys Asp Val Cys Lys Glu Gly Phe Tyr
    370                 375                 380

Asp Leu Ser Ala Glu Asp Pro Tyr Gly Cys Lys Ser Cys Ala Cys Asn
385                 390                 395                 400

Pro Leu Gly Thr Ile Pro Gly Gly Asn Pro Cys Asp Ser Glu Thr Gly
                405                 410                 415

Tyr Cys Tyr Cys Lys Arg Leu Val Thr Gly Gln Arg Cys Asp Gln Cys
            420                 425                 430
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Leu Pro Gln His Trp Gly Leu Ser Asn Asp Leu Asp Gly Cys Arg Pro
        435                 440                 445

Cys Asp Cys Asp Leu Gly Gly Ala Leu Asn Asn Ser Cys Ser Glu Asp
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Ser Gly Gln Cys Ser Cys Leu Pro His Met Ile Gly Arg Gln Cys Asn
465                 470                 475                 480

Glu Val Glu Ser Gly Tyr Tyr Phe Thr Thr Leu Asp His Tyr Ile Tyr
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Glu Ala Glu Glu Ala Asn Leu Gly Pro Gly Val Val Val Val Glu Arg
            500                 505                 510

Gln Tyr Ile Gln Asp Arg Ile Pro Ser Trp Thr Gly Pro Gly Phe Val
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Arg Val Pro Glu Gly Ala Tyr Leu Glu Phe Phe Ile Asp Asn Ile Pro
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Tyr Ser Met Glu Tyr Glu Ile Leu Ile Arg Tyr Glu Pro Gln Leu Pro
545                 550                 555                 560

Asp His Trp Glu Lys Ala Val Ile Thr Val Gln Arg Pro Gly Lys Ile
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Pro Ala Ser Ser Arg Cys Gly Asn Thr Val Pro Asp Asp Asp Asn Gln
            580                 585                 590

Val Val Ser Leu Ser Pro Gly Ser Arg Tyr Val Val Leu Pro Arg Pro
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Val Cys Phe Glu Lys Gly Met Asn Tyr Thr Val Arg Leu Glu Leu Pro
    610                 615                 620

Gln Tyr Thr Ala Ser Gly Ser Asp Val Glu Ser Pro Tyr Thr Phe Ile
625                 630                 635                 640

Asp Ser Leu Val Leu Met Pro Tyr Cys Lys Ser Leu Asp Ile Phe Thr
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Val Gly Gly Ser Gly Asp Gly Glu Val Thr Asn Ser Ala Trp Glu Thr
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Phe Gln Arg Tyr Arg Cys Leu Glu Asn Ser Arg Ser Val Val Lys Thr
        675                 680                 685

Pro Met Thr Asp Val Cys Arg Asn Ile Ile Phe Ser Ile Ser Ala Leu
    690                 695                 700

Ile His Gln Thr Gly Leu Ala Cys Glu Cys Asp Pro Gln Gly Ser Leu
705                 710                 715                 720

Ser Ser Val Cys Asp Pro Asn Gly Gly Gln Cys Gln Cys Arg Pro Asn
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Val Val Gly Arg Thr Cys Asn Arg Cys Ala Pro Gly Thr Phe Gly Phe
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Gly Pro Asn Gly Cys Lys Pro Cys Asp Cys His Leu Gln Gly Ser Ala
        755                 760                 765

Ser Ala Phe Cys Asp Ala Ile Thr Gly Gln Cys His Cys Phe Gln Gly
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Ile Tyr Ala Arg Gln Cys Asp Arg Cys Leu Pro Gly Tyr Trp Gly Phe
785                 790                 795                 800

Pro Ser Cys Gln Pro Cys Gln Cys Asn Gly His Ala Leu Asp Cys Asp
                805                 810                 815

Thr Val Thr Gly Glu Cys Leu Ser Cys Gln Asp Tyr Thr Thr Gly His
            820                 825                 830

Asn Cys Glu Arg Cys Leu Ala Gly Tyr Tyr Gly Asp Pro Ile Ile Gly
        835                 840                 845

Ser Gly Asp His Cys Arg Pro Cys Pro Cys Pro Asp Gly Pro Asp Ser
    850                 855                 860

Gly Arg Gln Phe Ala Arg Ser Cys Tyr Gln Asp Pro Val Thr Leu Gln
865                 870                 875                 880

Leu Ala Cys Val Cys Asp Pro Gly Tyr Ile Gly Ser Arg Cys Asp Asp
                885                 890                 895

Cys Ala Ser Gly Phe Phe Gly Asn Pro Ser Asp Phe Gly Gly Ser Cys
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Gln Pro Cys Gln Cys His His Asn Ile Asp Thr Thr Asp Pro Glu Ala
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Cys Asp Lys Asp Thr Gly Arg Cys Leu Lys Cys Leu Tyr His Thr Glu
    930                 935                 940

Gly Asp His Cys Gln Leu Cys Gln Tyr Gly Tyr Tyr Gly Asp Ala Leu
945                 950                 955                 960

Arg Gln Asp Cys Arg Lys Cys Val Cys Asn Tyr Leu Gly Thr Val Lys
                965                 970                 975

Glu His Cys Asn Gly Ser Asp Cys His Cys Asp Lys Ala Thr Gly Gln
            980                 985                 990

Cys Ser Cys Leu Pro Asn Val Ile Gly Gln Asn Cys Asp Arg Cys Ala
        995                1000                1005

Pro Asn Thr Trp Gln Leu Ala Ser Gly Thr Gly Cys Gly Pro Cys Asn
   1010                1015                1020

Cys Asn Ala Ala His Ser Phe Gly Pro Ser Cys Asn Glu Phe Thr Gly
1025                1030                1035                1040

Gln Cys Gln Cys Met Pro Gly Phe Gly Gly Arg Thr Cys Ser Glu Cys
                1045                1050                1055

Gln Glu Leu Phe Trp Gly Asp Pro Asp Val Glu Cys Arg Ala Cys Asp
            1060                1065                1070

Cys Asp Pro Arg Gly Ile Glu Thr Pro Gln Cys Asp Gln Ser Thr Gly
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Gln Cys Val Cys Val Glu Gly Val Glu Gly Pro Arg Cys Asp Lys Cys
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Thr Arg Gly Tyr Ser Gly Val Phe Pro Asp Cys Thr Pro Cys His Gln
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Cys Phe Ala Leu Trp Asp Ala Ile Ile Gly Glu Leu Thr Asn Arg Thr
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His Lys Phe Leu Glu Lys Ala Lys Ala Leu Lys Ile Ser Gly Val Ile
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Gly Pro Tyr Arg Glu Thr Val Asp Ser Val Glu Lys Lys Val Asn Glu
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Ile Lys Asp Ile Leu Ala Gln Ser Pro Ala Ala Glu Pro Leu Lys Asn
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Ile Gly Ile Leu Phe Glu Glu Ala Glu Lys Leu Thr Lys Asp Val Thr
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Glu Lys Met Ala Gln Val Glu Val Lys Leu Thr Asp Thr Ala Ser Gln
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Ser Asn Ser Thr Ala Gly Glu Leu Gly Ala Leu Gln Ala Glu Ala Glu
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Ser Leu Asp Lys Thr Val Lys Glu Leu Ala Glu Gln Leu Glu Phe Ile
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Lys Asn Ser Asp Ile Gln Gly Ala Leu Asp Ser Ile Thr Lys Tyr Phe
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Gln Met Ser Leu Glu Ala Glu Lys Arg Val Asn Ala Ser Thr Thr Asp
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Pro Asn Ser Thr Val Glu Gln Ser Ala Leu Thr Arg Asp Arg Val Glu
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Gln Ala Arg Leu Leu Asp Glu Leu Ala Gly Lys Leu Gln Ser Leu Asp
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Leu Ser Ala Ala Ala Gln Met Thr Cys Gly Thr Pro Pro Gly Ala Asp
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Cys Ser Glu Ser Glu Cys Gly Gly Pro Asn Cys Arg Thr Asp Glu Gly
1345 1350 1355 1360

Glu Lys Lys Cys Gly Gly Pro Gly Cys Gly Gly Leu Val Thr Val Ala
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His Ser Ala Trp Gln Lys Ala Met Asp Phe Asp Arg Asp Val Leu Ser
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Ala Leu Ala Glu Val Glu Gln Leu Ser Lys Met Val Ser Glu Ala Lys
1395 1400 1405

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Val Arg Ala Asp Glu Ala Lys Gln Asn Ala Gln Asp Val Leu Leu Lys
   1410                1415                1420

Thr Asn Ala Thr Lys Glu Lys Val Asp Lys Ser Asn Glu Asp Leu Arg
1425                1430                1435                1440

Asn Leu Ile Lys Gln Ile Arg Asn Phe Leu Thr Glu Asp Ser Ala Asp
                1445                1450                1455

Leu Asp Ser Ile Glu Ala Val Ala Asn Glu Val Leu Lys Ser Gly Asn
            1460                1465                1470

Ala Ser Thr Pro Gln Gln Leu Gln Asn Leu Thr Glu Asp Ile Arg Glu
        1475                1480                1485

Arg Val Glu Thr Leu Ser Gln Val Glu Val Ile Leu Gln Gln Ser Ala
   1490                1495                1500

Ala Asp Ile Ala Arg Ala Glu Leu Leu Leu Glu Glu Ala Lys Arg Ala
1505                1510                1515                1520

Ser Lys Ser Ala Thr Asp Val Lys Val Thr Ala Asp Met Val Lys Glu
                1525                1530                1535

Ala Leu Glu Glu Ala Glu Lys Ala Gln Val Ala Ala Glu Lys Ala Ile
            1540                1545                1550

Lys Gln Ala Asp Glu Asp Ile Gln Gly Thr Gln Asn Leu Leu Thr Ser
        1555                1560                1565

Ile Glu Ser Glu Thr Ala Ala Ser Glu Glu Thr Leu Thr Asn Ala Ser
   1570                1575                1580

Gln Arg Ile Ser Lys Leu Glu Arg Asn Val Glu Glu Leu Lys Arg Lys
1585                1590                1595                1600

Ala Ala Gln Asn Ser Gly Glu Ala Glu Tyr Ile Glu Lys Val Val Tyr
                1605                1610                1615

Ser Val Lys Gln Asn Ala Asp Asp Val Lys Lys Thr Leu Asp Gly Glu
            1620                1625                1630

Leu Asp Glu Lys Tyr Lys Lys Val Glu Ser Leu Ile Ala Gln Lys Thr
        1635                1640                1645

Glu Glu Ser Ala Asp Ala Arg Arg Lys Ala Glu Leu Leu Gln Asn Glu
   1650                1655                1660

Ala Lys Thr Leu Leu Ala Gln Ala Asn Ser Lys Leu Gln Leu Leu Glu
1665                1670                1675                1680

Asp Leu Glu Arg Lys Tyr Glu Asp Asn Gln Lys Tyr Leu Glu Asp Lys
                1685                1690                1695

Ala Gln Glu Leu Val Arg Leu Glu Gly Glu Val Arg Ser Leu Leu Lys
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Asp Ile Ser Glu Lys Val Ala Val Tyr Ser Thr Cys Leu
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gcctccgggg gacgccgcta ggcgagagga acgcgccggt gcccttgcct tcgccgtgac 240

ccagcgtgcg ggcggcggg atg aga ggg agc cat cgg gcc gcg ccg gcc ctg 292
Met Arg Gly Ser His Arg Ala Ala Pro Ala Leu
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cgg ccc cgg ggg cgg ctc tgg ccc gtg ctg gcc gtg ctg gcg gcg gcc 340
Arg Pro Arg Gly Arg Leu Trp Pro Val Leu Ala Val Leu Ala Ala Ala
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gcc gcg gcg ggc tgt gcc cag gca gcc atg gac gag tgc acg gac gag 388
Ala Ala Ala Gly Cys Ala Gln Ala Ala Met Asp Glu Cys Thr Asp Glu
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ggc ggg cgg ccg cag cgc tgc atg ccc gag ttc gtc aac gcc gct ttc 436
Gly Gly Arg Pro Gln Arg Cys Met Pro Glu Phe Val Asn Ala Ala Phe
45 50 55

aac gtg act gtg gtg gcc acc aac acg tgt ggg act ccg ccc gag gaa 484
Asn Val Thr Val Val Ala Thr Asn Thr Cys Gly Thr Pro Pro Glu Glu
60 65 70 75

tac tgt gtg cag acc ggg gtg acc ggg gtc acc aag tcc tgt cac ctg 532
Tyr Cys Val Gln Thr Gly Val Thr Gly Val Thr Lys Ser Cys His Leu
80 85 90

tgc gac gcc ggg cag ccc cac ctg cag cac ggg gca gcc ttc ctg acc 580
Cys Asp Ala Gly Gln Pro His Leu Gln His Gly Ala Ala Phe Leu Thr
95 100 105

gac tac aac aac cag gcc gac acc acc tgg tgg caa agc cag acc atg 628
Asp Tyr Asn Asn Gln Ala Asp Thr Thr Trp Trp Gln Ser Gln Thr Met
110 115 120

ctg gcc ggg gtg cag tac ccc agc tcc atc aac ctc acg ctg cac ctg 676
Leu Ala Gly Val Gln Tyr Pro Ser Ser Ile Asn Leu Thr Leu His Leu
125 130 135

gga aaa gct ttt gac atc acc tat gtg cgt ctc aag ttc cac acc agc 724
Gly Lys Ala Phe Asp Ile Thr Tyr Val Arg Leu Lys Phe His Thr Ser

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140                 145                 150                 155

cgc ccg gag agc ttt gcc att tac aag cgc aca cgg gaa gac ggg ccc   772
Arg Pro Glu Ser Phe Ala Ile Tyr Lys Arg Thr Arg Glu Asp Gly Pro
                160                 165                 170

tgg att cct tac cag tac tac agt ggt tcc tgc gag aac acc tac tcc   820
Trp Ile Pro Tyr Gln Tyr Tyr Ser Gly Ser Cys Glu Asn Thr Tyr Ser
            175                 180                 185

aag gca aac cgc ggc ttc atc agg aca gga ggg gac gag cag cag gcc   868
Lys Ala Asn Arg Gly Phe Ile Arg Thr Gly Gly Asp Glu Gln Gln Ala
        190                 195                 200

ttg tgt act gat gaa ttc agt gac att tct ccc ctc act ggg ggc aac   916
Leu Cys Thr Asp Glu Phe Ser Asp Ile Ser Pro Leu Thr Gly Gly Asn
    205                 210                 215

gtg gcc ttt tct acc ctg gaa gga agg ccc agc gcc tat aac ttt gac   964
Val Ala Phe Ser Thr Leu Glu Gly Arg Pro Ser Ala Tyr Asn Phe Asp
220                 225                 230                 235

aat agc cct gtg ctg cag gaa tgg gta act gcc act gac atc aga gta   1012
Asn Ser Pro Val Leu Gln Glu Trp Val Thr Ala Thr Asp Ile Arg Val
                240                 245                 250

act ctt aat cgc ctg aac act ttt gga gat gaa gtg ttt aac gat ccc   1060
Thr Leu Asn Arg Leu Asn Thr Phe Gly Asp Glu Val Phe Asn Asp Pro
            255                 260                 265

aaa gtt ctc aag tcc tat tat tat gcc atc tct gat ttt gct gta ggt   1108
Lys Val Leu Lys Ser Tyr Tyr Tyr Ala Ile Ser Asp Phe Ala Val Gly
        270                 275                 280

ggc aga tgt aaa tgt aat gga cac gca agc gag tgt atg aag aac gaa   1156
Gly Arg Cys Lys Cys Asn Gly His Ala Ser Glu Cys Met Lys Asn Glu
    285                 290                 295

ttt gat aag ctg gtg tgt aat tgc aaa cat aac aca tat gga gta gac   1204
Phe Asp Lys Leu Val Cys Asn Cys Lys His Asn Thr Tyr Gly Val Asp
300                 305                 310                 315

tgt gaa aag tgt ctt cct ttc ttc aat gac cgg ccg tgg agg agg gca   1252
Cys Glu Lys Cys Leu Pro Phe Phe Asn Asp Arg Pro Trp Arg Arg Ala
                320                 325                 330

act gcg gaa agt gcc agt gaa tgc ctg ccc tgt gat tgc aat ggt cga   1300
Thr Ala Glu Ser Ala Ser Glu Cys Leu Pro Cys Asp Cys Asn Gly Arg
            335                 340                 345

tcc cag gaa tgc tac ttc gac cct gaa ctc tat cgt tcc act ggc cat   1348
Ser Gln Glu Cys Tyr Phe Asp Pro Glu Leu Tyr Arg Ser Thr Gly His
        350                 355                 360

ggg ggc cac tgt acc aac tgc cag gat aac aca gat ggc gcc cac tgt   1396
Gly Gly His Cys Thr Asn Cys Gln Asp Asn Thr Asp Gly Ala His Cys
    365                 370                 375

gag agg tgc cga gag aac ttc ttc cgc ctt ggc aac aat gaa gcc tgc   1444
Glu Arg Cys Arg Glu Asn Phe Phe Arg Leu Gly Asn Asn Glu Ala Cys
380                 385                 390                 395
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tct tca tgc cac tgt agt cct gtg ggc tct cta agc aca cag tgt gat   1492
Ser Ser Cys His Cys Ser Pro Val Gly Ser Leu Ser Thr Gln Cys Asp
                400                 405                 410

agt tac ggc aga tgc agc tgt aag cca gga gtg atg ggg gac aaa tgt   1540
Ser Tyr Gly Arg Cys Ser Cys Lys Pro Gly Val Met Gly Asp Lys Cys
            415                 420                 425

gac cgt tgc cag cct gga ttc cat tct ctc act gaa gca gga tgc agg   1588
Asp Arg Cys Gln Pro Gly Phe His Ser Leu Thr Glu Ala Gly Cys Arg
        430                 435                 440

cca tgc tct tgt gat ccc tct ggc agc ata gat gaa tgt aat gtt gaa   1636
Pro Cys Ser Cys Asp Pro Ser Gly Ser Ile Asp Glu Cys Asn Val Glu
    445                 450                 455

aca gga aga tgt gtt tgc aaa gac aat gtc gaa ggc ttc aat tgt gaa   1684
Thr Gly Arg Cys Val Cys Lys Asp Asn Val Glu Gly Phe Asn Cys Glu
460                 465                 470                 475

aga tgc aaa cct gga ttt ttt aat ctg gaa tca tct aat cct cgg ggt   1732
Arg Cys Lys Pro Gly Phe Phe Asn Leu Glu Ser Ser Asn Pro Arg Gly
                480                 485                 490

tgc aca ccc tgc ttc tgc ttt ggg cat tct tct gtc tgt aca aac gct   1780
Cys Thr Pro Cys Phe Cys Phe Gly His Ser Ser Val Cys Thr Asn Ala
            495                 500                 505

gtt ggc tac agt gtt tat tct atc tcc tct acc ttt cag att gat gag   1828
Val Gly Tyr Ser Val Tyr Ser Ile Ser Ser Thr Phe Gln Ile Asp Glu
        510                 515                 520

gat ggg tgg cgt gcg gaa cag aga gat ggc tct gaa gca tct ctc gag   1876
Asp Gly Trp Arg Ala Glu Gln Arg Asp Gly Ser Glu Ala Ser Leu Glu
    525                 530                 535

tgg tcc tct gag agg caa gat atc gcc gtg atc tca gac agc tac ttt   1924
Trp Ser Ser Glu Arg Gln Asp Ile Ala Val Ile Ser Asp Ser Tyr Phe
540                 545                 550                 555

cct cgg tac ttc att gct cct gca aag ttc ttg ggc aag cag gtg ttg   1972
Pro Arg Tyr Phe Ile Ala Pro Ala Lys Phe Leu Gly Lys Gln Val Leu
                560                 565                 570

agt tat ggt cag aac ctc tcc ttc tcc ttt cga gtg gac agg cga gat   2020
Ser Tyr Gly Gln Asn Leu Ser Phe Ser Phe Arg Val Asp Arg Arg Asp
            575                 580                 585

act cgc ctc tct gcc gaa gac ctt gtg ctt gag gga gct ggc tta aga   2068
Thr Arg Leu Ser Ala Glu Asp Leu Val Leu Glu Gly Ala Gly Leu Arg
        590                 595                 600

gta tct gta ccc ttg atc gct cag ggc aat tcc tat cca agt gag acc   2116
Val Ser Val Pro Leu Ile Ala Gln Gly Asn Ser Tyr Pro Ser Glu Thr
    605                 610                 615

act gtg aag tat gtc ttc agg ctc cat gaa gca aca gat tac cct tgg   2164
Thr Val Lys Tyr Val Phe Arg Leu His Glu Ala Thr Asp Tyr Pro Trp
620                 625                 630                 635
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agg cct gct ctt acc cct ttt gaa ttt cag aag ctc cta aac aac ttg   2212
Arg Pro Ala Leu Thr Pro Phe Glu Phe Gln Lys Leu Leu Asn Asn Leu
                640                 645                 650

acc tct atc aag ata cgt ggg aca tac agt gag aga agt gct gga tat   2260
Thr Ser Ile Lys Ile Arg Gly Thr Tyr Ser Glu Arg Ser Ala Gly Tyr
            655                 660                 665

ttg gat gat gtc acc ctg gca agt gct cgt cct ggg cct gga gtc cct   2308
Leu Asp Asp Val Thr Leu Ala Ser Ala Arg Pro Gly Pro Gly Val Pro
        670                 675                 680

gca act tgg gtg gag tcc tgc acc tgt cct gtg gga tat gga ggg cag   2356
Ala Thr Trp Val Glu Ser Cys Thr Cys Pro Val Gly Tyr Gly Gly Gln
    685                 690                 695

ttt tgt gag atg tgc ctc tca ggt tac aga aga gaa act cct aat ctt   2404
Phe Cys Glu Met Cys Leu Ser Gly Tyr Arg Arg Glu Thr Pro Asn Leu
700                 705                 710                 715

gga cca tac agt cca tgt gtg ctt tgc gcc tgc aat gga cac agc gag   2452
Gly Pro Tyr Ser Pro Cys Val Leu Cys Ala Cys Asn Gly His Ser Glu
                720                 725                 730

acc tgt gat cct gag aca ggt gtt tgt aac tgc aga gac aat acg gct   2500
Thr Cys Asp Pro Glu Thr Gly Val Cys Asn Cys Arg Asp Asn Thr Ala
            735                 740                 745

ggc ccg cac tgt gag aag tgc agt gat ggg tac tat gga gat tca act   2548
Gly Pro His Cys Glu Lys Cys Ser Asp Gly Tyr Tyr Gly Asp Ser Thr
        750                 755                 760

gca ggc acc tcc tcc gat tgc caa ccc tgt ccg tgt cct gga ggt tca   2596
Ala Gly Thr Ser Ser Asp Cys Gln Pro Cys Pro Cys Pro Gly Gly Ser
    765                 770                 775

agt tgt gct gtt gtt ccc aag aca aag gag gtg gtg tgc acc aac tgt   2644
Ser Cys Ala Val Val Pro Lys Thr Lys Glu Val Val Cys Thr Asn Cys
780                 785                 790                 795

cct act ggc acc act ggt aag aga tgt gag ctc tgt gat gat ggc tac   2692
Pro Thr Gly Thr Thr Gly Lys Arg Cys Glu Leu Cys Asp Asp Gly Tyr
                800                 805                 810

ttt gga gac ccc ctg ggt aga aac ggc cct gtg aga ctt tgc cgc ctg   2740
Phe Gly Asp Pro Leu Gly Arg Asn Gly Pro Val Arg Leu Cys Arg Leu
            815                 820                 825

tgc cag tgc agt gac aac atc gat ccc aac gca gtt gga aat tgc aat   2788
Cys Gln Cys Ser Asp Asn Ile Asp Pro Asn Ala Val Gly Asn Cys Asn
        830                 835                 840

cgc ttg acg gga gaa tgc ctg aag tgc atc tat aac act gct ggc ttc   2836
Arg Leu Thr Gly Glu Cys Leu Lys Cys Ile Tyr Asn Thr Ala Gly Phe
    845                 850                 855

tat tgt gac cgg tgc aaa gac gga ttt ttt gga aat ccc ctg gct ccc   2884
Tyr Cys Asp Arg Cys Lys Asp Gly Phe Phe Gly Asn Pro Leu Ala Pro
860                 865                 870                 875

aat cca gca gac aaa tgc aaa gcc tgc aat tgc aat ccg tat ggg acc   2932
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                880                 885                 890

atg aag cag cag agc agc tgt aac ccc gtg acg ggg cag tgt gaa tgt   2980
Met Lys Gln Gln Ser Ser Cys Asn Pro Val Thr Gly Gln Cys Glu Cys
            895                 900                 905

ttg cct cac gtg act ggc cag gac tgt ggt gct tgt gac cct gga ttc   3028
Leu Pro His Val Thr Gly Gln Asp Cys Gly Ala Cys Asp Pro Gly Phe
        910                 915                 920

tac aat ctg cag agt ggg caa ggc tgt gag agg tgt gac tgc cat gcc   3076
Tyr Asn Leu Gln Ser Gly Gln Gly Cys Glu Arg Cys Asp Cys His Ala
    925                 930                 935

ttg ggc tcc acc aat ggg cag tgt gac atc cgc acc ggc cag tgt gag   3124
Leu Gly Ser Thr Asn Gly Gln Cys Asp Ile Arg Thr Gly Gln Cys Glu
940                 945                 950                 955

tgc cag ccc ggc atc act ggt cag cac tgt gag cgc tgt gag gtc aac   3172
Cys Gln Pro Gly Ile Thr Gly Gln His Cys Glu Arg Cys Glu Val Asn
                960                 965                 970

cac ttt ggg ttt gga cct gaa ggc tgc aaa ccc tgt gac tgt cat cct   3220
His Phe Gly Phe Gly Pro Glu Gly Cys Lys Pro Cys Asp Cys His Pro
            975                 980                 985

gag gga tct ctt tca ctt cag tgc aaa gat gat ggt cgc tgt gaa tgc   3268
Glu Gly Ser Leu Ser Leu Gln Cys Lys Asp Asp Gly Arg Cys Glu Cys
        990                 995                1000

aga gaa ggc ttt gtg gga aat cgc tgt gac cag tgt gaa gaa aac tat   3316
Arg Glu Gly Phe Val Gly Asn Arg Cys Asp Gln Cys Glu Glu Asn Tyr
   1005                1010                1015

ttc tac aat cgg tct tgg cct ggc tgc cag gaa tgt cca gct tgt tac   3364
Phe Tyr Asn Arg Ser Trp Pro Gly Cys Gln Glu Cys Pro Ala Cys Tyr
1020                1025                1030                1035

cgg ctg gta aag gat aag gtt gct gat cat aga gtg aag ctc cag gaa   3412
Arg Leu Val Lys Asp Lys Val Ala Asp His Arg Val Lys Leu Gln Glu
               1040                1045                1050

tta gag agt ctc ata gca aac ctt gga act ggg gat gag atg gtg aca   3460
Leu Glu Ser Leu Ile Ala Asn Leu Gly Thr Gly Asp Glu Met Val Thr
           1055                1060                1065

gat caa gcc ttc gag gat aga cta aag gaa gca gag agg gaa gtt atg   3508
Asp Gln Ala Phe Glu Asp Arg Leu Lys Glu Ala Glu Arg Glu Val Met
       1070                1075                1080

gac ctc ctt cgt gag gcc cag gat gtc aaa gat gtt gac cag aat ttg   3556
Asp Leu Leu Arg Glu Ala Gln Asp Val Lys Asp Val Asp Gln Asn Leu
   1085                1090                1095

atg gat cgc cta cag aga gtg aat aac act ctg tcc agc caa att agc   3604
Met Asp Arg Leu Gln Arg Val Asn Asn Thr Leu Ser Ser Gln Ile Ser
1100                1105                1110                1115

cgt tta cag aat atc cgg aat acc att gaa gag act gga aac ttg gct   3652
Arg Leu Gln Asn Ile Arg Asn Thr Ile Glu Glu Thr Gly Asn Leu Ala
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          1135                1140                1145

gca tcc aga gaa ctt gag aaa gca aaa gtc gct gct gcc aat gtg tca   3748
Ala Ser Arg Glu Leu Glu Lys Ala Lys Val Ala Ala Ala Asn Val Ser
       1150                1155                1160

gtc act cag cca gaa tct aca ggg gac cca aac aac atg act ctt ttg   3796
Val Thr Gln Pro Glu Ser Thr Gly Asp Pro Asn Asn Met Thr Leu Leu
   1165                1170                1175

gca gaa gag gct cga aag ctt gct gaa cgt cat aaa cag gaa gct gat   3844
Ala Glu Glu Ala Arg Lys Leu Ala Glu Arg His Lys Gln Glu Ala Asp
1180                1185                1190                1195

gac att gtt cga gtg gca aag aca gcc aat gat acg tca act gag gca   3892
Asp Ile Val Arg Val Ala Lys Thr Ala Asn Asp Thr Ser Thr Glu Ala
               1200                1205                1210

tac aac ctg ctt ctg agg aca ctg gca gga gaa aat caa aca gca ttt   3940
Tyr Asn Leu Leu Leu Arg Thr Leu Ala Gly Glu Asn Gln Thr Ala Phe
          1215                1220                1225

gag att gaa gag ctt aat agg aag tat gaa caa gcg aag aac atc tca   3988
Glu Ile Glu Glu Leu Asn Arg Lys Tyr Glu Gln Ala Lys Asn Ile Ser
       1230                1235                1240

cag gat ctg gaa aaa caa gct gcc cga gta cat gag gag gcc aaa agg   4036
Gln Asp Leu Glu Lys Gln Ala Ala Arg Val His Glu Glu Ala Lys Arg
   1245                1250                1255

gcc ggt gac aaa gct gtg gag atc tat gcc agc gtg gct cag ctg agc   4084
Ala Gly Asp Lys Ala Val Glu Ile Tyr Ala Ser Val Ala Gln Leu Ser
1260                1265                1270                1275

cct ttg gac tct gag aca ctg gag aat gaa gca aat aac ata aag atg   4132
Pro Leu Asp Ser Glu Thr Leu Glu Asn Glu Ala Asn Asn Ile Lys Met
               1280                1285                1290

gaa gct gag aat ctg gaa caa ctg att gac cag aaa tta aaa gat tat   4180
Glu Ala Glu Asn Leu Glu Gln Leu Ile Asp Gln Lys Leu Lys Asp Tyr
          1295                1300                1305

gag gac ctc aga gaa gat atg aga ggg aag gaa ctt gaa gtc aag aac   4228
Glu Asp Leu Arg Glu Asp Met Arg Gly Lys Glu Leu Glu Val Lys Asn
       1310                1315                1320

ctt ctg gag aaa ggc aag act gaa cag cag acc gca gac caa ctc cta   4276
Leu Leu Glu Lys Gly Lys Thr Glu Gln Gln Thr Ala Asp Gln Leu Leu
   1325                1330                1335

gcc cga gct gat gct gcc aag gcc ctc gct gaa gaa gct gca aag aag   4324
Ala Arg Ala Asp Ala Ala Lys Ala Leu Ala Glu Glu Ala Ala Lys Lys
1340                1345                1350                1355

gga cgg gat acc tta caa gaa gct aat gac att ctc aac aac ctg aaa   4372
Gly Arg Asp Thr Leu Gln Glu Ala Asn Asp Ile Leu Asn Asn Leu Lys
               1360                1365                1370
```

```
gat ttt gat agg cgc gtg aac gat aac aag acg gcc gca gag gag gca   4420
Asp Phe Asp Arg Arg Val Asn Asp Asn Lys Thr Ala Ala Glu Glu Ala
          1375                1380                1385

cta agg aag att cct gcc atc aac cag acc atc act gaa gcc aat gaa   4468
Leu Arg Lys Ile Pro Ala Ile Asn Gln Thr Ile Thr Glu Ala Asn Glu
      1390                1395                1400

aag acc aga gaa gcc cag cag gcc ctg ggc agt gct gcg gcg gat gcc   4516
Lys Thr Arg Glu Ala Gln Gln Ala Leu Gly Ser Ala Ala Ala Asp Ala
   1405                1410                1415

aca gag gcc aag aac aag gcc cat gag gcg gag agg atc gca agc gct   4564
Thr Glu Ala Lys Asn Lys Ala His Glu Ala Glu Arg Ile Ala Ser Ala
1420                1425                1430                1435

gtc caa aag aat gcc acc agc acc aag gca gaa gct gaa aga act ttt   4612
Val Gln Lys Asn Ala Thr Ser Thr Lys Ala Glu Ala Glu Arg Thr Phe
               1440                1445                1450

gca gaa gtt aca gat ctg gat aat gag gtg aac aat atg ttg aag caa   4660
Ala Glu Val Thr Asp Leu Asp Asn Glu Val Asn Asn Met Leu Lys Gln
          1455                1460                1465

ctg cag gaa gca gaa aaa gag cta aag aga aaa caa gat gac gct gac   4708
Leu Gln Glu Ala Glu Lys Glu Leu Lys Arg Lys Gln Asp Asp Ala Asp
      1470                1475                1480

cag gac atg atg atg gca ggg atg gct tca cag gct gct caa gaa gcc   4756
Gln Asp Met Met Met Ala Gly Met Ala Ser Gln Ala Ala Gln Glu Ala
   1485                1490                1495

gag atc aat gcc aga aaa gcc aaa aac tct gtt act agc ctc ctc agc   4804
Glu Ile Asn Ala Arg Lys Ala Lys Asn Ser Val Thr Ser Leu Leu Ser
1500                1505                1510                1515

att att aat gac ctc ttg gag cag ctg ggg cag ctg gat aca gtg gac   4852
Ile Ile Asn Asp Leu Leu Glu Gln Leu Gly Gln Leu Asp Thr Val Asp
               1520                1525                1530

ctg aat aag cta aac gag att gaa ggc acc cta aac aaa gcc aaa gat   4900
Leu Asn Lys Leu Asn Glu Ile Glu Gly Thr Leu Asn Lys Ala Lys Asp
          1535                1540                1545

gaa atg aag gtc agc gat ctt gat agg aaa gtg tct gac ctg gag aat   4948
Glu Met Lys Val Ser Asp Leu Asp Arg Lys Val Ser Asp Leu Glu Asn
      1550                1555                1560

gaa gcc aag aag cag gag gct gcc atc atg gac tat aac cga gat atc   4996
Glu Ala Lys Lys Gln Glu Ala Ala Ile Met Asp Tyr Asn Arg Asp Ile
   1565                1570                1575

gag gag atc atg aag gac att cgc aat ctg gag gac atc agg aag acc   5044
Glu Glu Ile Met Lys Asp Ile Arg Asn Leu Glu Asp Ile Arg Lys Thr
1580                1585                1590                1595

tta cca tct ggc tgc ttc aac acc ccg tcc att gaa aag ccc           5086
Leu Pro Ser Gly Cys Phe Asn Thr Pro Ser Ile Glu Lys Pro
               1600                1605
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tagtgtcttt agggctggaa ggcagcatcc ctctgacagg ggggcagttg tgaggccaca 5146

gagtgccttg acacaaagat tacatttttc agacccccac tcctctgctg ctgtccatca 5206

ctgtcctttt gaaccaggaa aagtcacaga gtttaaagag aagcaaatta aacatcctga 5266

atcgggaaca aagggtttta tctaataaag tgtctcttcc 5306

<210> 22
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Met Arg Gly Ser His Arg Ala Ala Pro Ala Leu Arg Pro Arg Gly Arg
  1               5                  10                  15

Leu Trp Pro Val Leu Ala Val Leu Ala Ala Ala Ala Ala Ala Gly Cys
             20                  25                  30

Ala Gln Ala Ala Met Asp Glu Cys Thr Asp Glu Gly Gly Arg Pro Gln
         35                  40                  45

Arg Cys Met Pro Glu Phe Val Asn Ala Ala Phe Asn Val Thr Val Val
     50                  55                  60

Ala Thr Asn Thr Cys Gly Thr Pro Pro Glu Glu Tyr Cys Val Gln Thr
 65                  70                  75                  80

Gly Val Thr Gly Val Thr Lys Ser Cys His Leu Cys Asp Ala Gly Gln
                 85                  90                  95

Pro His Leu Gln His Gly Ala Ala Phe Leu Thr Asp Tyr Asn Asn Gln
            100                 105                 110

Ala Asp Thr Thr Trp Trp Gln Ser Gln Thr Met Leu Ala Gly Val Gln
        115                 120                 125

Tyr Pro Ser Ser Ile Asn Leu Thr Leu His Leu Gly Lys Ala Phe Asp
    130                 135                 140

Ile Thr Tyr Val Arg Leu Lys Phe His Thr Ser Arg Pro Glu Ser Phe
145                 150                 155                 160

Ala Ile Tyr Lys Arg Thr Arg Glu Asp Gly Pro Trp Ile Pro Tyr Gln
                165                 170                 175

Tyr Tyr Ser Gly Ser Cys Glu Asn Thr Tyr Ser Lys Ala Asn Arg Gly
            180                 185                 190

Phe Ile Arg Thr Gly Gly Asp Glu Gln Gln Ala Leu Cys Thr Asp Glu
        195                 200                 205

Phe Ser Asp Ile Ser Pro Leu Thr Gly Gly Asn Val Ala Phe Ser Thr
    210                 215                 220

Leu Glu Gly Arg Pro Ser Ala Tyr Asn Phe Asp Asn Ser Pro Val Leu
225                 230                 235                 240

Gln Glu Trp Val Thr Ala Thr Asp Ile Arg Val Thr Leu Asn Arg Leu
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245 250 255

Asn Thr Phe Gly Asp Glu Val Phe Asn Asp Pro Lys Val Leu Lys Ser
260 265 270

Tyr Tyr Tyr Ala Ile Ser Asp Phe Ala Val Gly Gly Arg Cys Lys Cys
275 280 285

Asn Gly His Ala Ser Glu Cys Met Lys Asn Glu Phe Asp Lys Leu Val
290 295 300

Cys Asn Cys Lys His Asn Thr Tyr Gly Val Asp Cys Glu Lys Cys Leu
305 310 315 320

Pro Phe Phe Asn Asp Arg Pro Trp Arg Arg Ala Thr Ala Glu Ser Ala
325 330 335

Ser Glu Cys Leu Pro Cys Asp Cys Asn Gly Arg Ser Gln Glu Cys Tyr
340 345 350

Phe Asp Pro Glu Leu Tyr Arg Ser Thr Gly His Gly Gly His Cys Thr
355 360 365

Asn Cys Gln Asp Asn Thr Asp Gly Ala His Cys Glu Arg Cys Arg Glu
370 375 380

Asn Phe Phe Arg Leu Gly Asn Asn Glu Ala Cys Ser Ser Cys His Cys
385 390 395 400

Ser Pro Val Gly Ser Leu Ser Thr Gln Cys Asp Ser Tyr Gly Arg Cys
405 410 415

Ser Cys Lys Pro Gly Val Met Gly Asp Lys Cys Asp Arg Cys Gln Pro
420 425 430

Gly Phe His Ser Leu Thr Glu Ala Gly Cys Arg Pro Cys Ser Cys Asp
435 440 445

Pro Ser Gly Ser Ile Asp Glu Cys Asn Val Glu Thr Gly Arg Cys Val
450 455 460

Cys Lys Asp Asn Val Glu Gly Phe Asn Cys Glu Arg Cys Lys Pro Gly
465 470 475 480

Phe Phe Asn Leu Glu Ser Ser Asn Pro Arg Gly Cys Thr Pro Cys Phe
485 490 495

Cys Phe Gly His Ser Ser Val Cys Thr Asn Ala Val Gly Tyr Ser Val
500 505 510

Tyr Ser Ile Ser Ser Thr Phe Gln Ile Asp Glu Asp Gly Trp Arg Ala
515 520 525

Glu Gln Arg Asp Gly Ser Glu Ala Ser Leu Glu Trp Ser Ser Glu Arg
530 535 540

Gln Asp Ile Ala Val Ile Ser Asp Ser Tyr Phe Pro Arg Tyr Phe Ile
545 550 555 560

Ala Pro Ala Lys Phe Leu Gly Lys Gln Val Leu Ser Tyr Gly Gln Asn
565 570 575

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Leu Ser Phe Ser Phe Arg Val Asp Arg Arg Asp Thr Arg Leu Ser Ala
            580                 585                 590

Glu Asp Leu Val Leu Glu Gly Ala Gly Leu Arg Val Ser Val Pro Leu
        595                 600                 605

Ile Ala Gln Gly Asn Ser Tyr Pro Ser Glu Thr Thr Val Lys Tyr Val
    610                 615                 620

Phe Arg Leu His Glu Ala Thr Asp Tyr Pro Trp Arg Pro Ala Leu Thr
625                 630                 635                 640

Pro Phe Glu Phe Gln Lys Leu Leu Asn Asn Leu Thr Ser Ile Lys Ile
                645                 650                 655

Arg Gly Thr Tyr Ser Glu Arg Ser Ala Gly Tyr Leu Asp Asp Val Thr
            660                 665                 670

Leu Ala Ser Ala Arg Pro Gly Pro Gly Val Pro Ala Thr Trp Val Glu
        675                 680                 685

Ser Cys Thr Cys Pro Val Gly Tyr Gly Gly Gln Phe Cys Glu Met Cys
    690                 695                 700

Leu Ser Gly Tyr Arg Arg Glu Thr Pro Asn Leu Gly Pro Tyr Ser Pro
705                 710                 715                 720

Cys Val Leu Cys Ala Cys Asn Gly His Ser Glu Thr Cys Asp Pro Glu
                725                 730                 735

Thr Gly Val Cys Asn Cys Arg Asp Asn Thr Ala Gly Pro His Cys Glu
            740                 745                 750

Lys Cys Ser Asp Gly Tyr Tyr Gly Asp Ser Thr Ala Gly Thr Ser Ser
        755                 760                 765

Asp Cys Gln Pro Cys Pro Cys Pro Gly Gly Ser Ser Cys Ala Val Val
    770                 775                 780

Pro Lys Thr Lys Glu Val Val Cys Thr Asn Cys Pro Thr Gly Thr Thr
785                 790                 795                 800

Gly Lys Arg Cys Glu Leu Cys Asp Asp Gly Tyr Phe Gly Asp Pro Leu
                805                 810                 815

Gly Arg Asn Gly Pro Val Arg Leu Cys Arg Leu Cys Gln Cys Ser Asp
            820                 825                 830

Asn Ile Asp Pro Asn Ala Val Gly Asn Cys Asn Arg Leu Thr Gly Glu
        835                 840                 845

Cys Leu Lys Cys Ile Tyr Asn Thr Ala Gly Phe Tyr Cys Asp Arg Cys
    850                 855                 860

Lys Asp Gly Phe Phe Gly Asn Pro Leu Ala Pro Asn Pro Ala Asp Lys
865                 870                 875                 880

Cys Lys Ala Cys Asn Cys Asn Pro Tyr Gly Thr Met Lys Gln Gln Ser
                885                 890                 895
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Ser Cys Asn Pro Val Thr Gly Gln Cys Glu Cys Leu Pro His Val Thr
            900                 905                 910

Gly Gln Asp Cys Gly Ala Cys Asp Pro Gly Phe Tyr Asn Leu Gln Ser
        915                 920                 925

Gly Gln Gly Cys Glu Arg Cys Asp Cys His Ala Leu Gly Ser Thr Asn
    930                 935                 940

Gly Gln Cys Asp Ile Arg Thr Gly Gln Cys Glu Cys Gln Pro Gly Ile
945                 950                 955                 960

Thr Gly Gln His Cys Glu Arg Cys Glu Val Asn His Phe Gly Phe Gly
                965                 970                 975

Pro Glu Gly Cys Lys Pro Cys Asp Cys His Pro Glu Gly Ser Leu Ser
            980                 985                 990

Leu Gln Cys Lys Asp Asp Gly Arg Cys Glu Cys Arg Glu Gly Phe Val
        995                1000                1005

Gly Asn Arg Cys Asp Gln Cys Glu Glu Asn Tyr Phe Tyr Asn Arg Ser
   1010                1015                1020

Trp Pro Gly Cys Gln Glu Cys Pro Ala Cys Tyr Arg Leu Val Lys Asp
025                1030                1035                1040

Lys Val Ala Asp His Arg Val Lys Leu Gln Glu Leu Glu Ser Leu Ile
               1045                1050                1055

Ala Asn Leu Gly Thr Gly Asp Glu Met Val Thr Asp Gln Ala Phe Glu
           1060                1065                1070

Asp Arg Leu Lys Glu Ala Glu Arg Glu Val Met Asp Leu Leu Arg Glu
       1075                1080                1085

Ala Gln Asp Val Lys Asp Val Asp Gln Asn Leu Met Asp Arg Leu Gln
   1090                1095                1100

Arg Val Asn Asn Thr Leu Ser Ser Gln Ile Ser Arg Leu Gln Asn Ile
105                1110                1115                1120

Arg Asn Thr Ile Glu Glu Thr Gly Asn Leu Ala Glu Gln Ala Arg Ala
               1125                1130                1135

His Val Glu Asn Thr Glu Arg Leu Ile Glu Ile Ala Ser Arg Glu Leu
           1140                1145                1150

Glu Lys Ala Lys Val Ala Ala Ala Asn Val Ser Val Thr Gln Pro Glu
       1155                1160                1165

Ser Thr Gly Asp Pro Asn Asn Met Thr Leu Leu Ala Glu Glu Ala Arg
   1170                1175                1180

Lys Leu Ala Glu Arg His Lys Gln Glu Ala Asp Asp Ile Val Arg Val
185                1190                1195                1200

Ala Lys Thr Ala Asn Asp Thr Ser Thr Glu Ala Tyr Asn Leu Leu Leu
               1205                1210                1215

Arg Thr Leu Ala Gly Glu Asn Gln Thr Ala Phe Glu Ile Glu Glu Leu
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gca agt gct cgt cct ggg cct gga gtc cct gca act tgg gtg gag tcc   1968
Ala Ser Ala Arg Pro Gly Pro Gly Val Pro Ala Thr Trp Val Glu Ser
                645                 650                 655

tgc acc tgt cct gtg gga tat gga ggg cag ttt tgt gag atg tgc ctc   2016
Cys Thr Cys Pro Val Gly Tyr Gly Gly Gln Phe Cys Glu Met Cys Leu
            660                 665                 670

tca ggt tac aga aga gaa act cct aat ctt gga cca tac agt cca tgt   2064
Ser Gly Tyr Arg Arg Glu Thr Pro Asn Leu Gly Pro Tyr Ser Pro Cys
        675                 680                 685

gtg ctt tgc gcc tgc aat gga cac agc gag acc tgt gat cct gag aca   2112
Val Leu Cys Ala Cys Asn Gly His Ser Glu Thr Cys Asp Pro Glu Thr
    690                 695                 700

ggt gtt tgt aac tgc aga gac aat acg gct ggc ccg cac tgt gag aag   2160
Gly Val Cys Asn Cys Arg Asp Asn Thr Ala Gly Pro His Cys Glu Lys
705                 710                 715                 720

tgc agt gat ggg tac tat gga gat tca act gca ggc acc tcc tcc gat   2208
Cys Ser Asp Gly Tyr Tyr Gly Asp Ser Thr Ala Gly Thr Ser Ser Asp
                725                 730                 735

tgc caa ccc tgt ccg tgt cct gga ggt tca agt tgt gct gtt gtt ccc   2256
Cys Gln Pro Cys Pro Cys Pro Gly Gly Ser Ser Cys Ala Val Val Pro
            740                 745                 750

aag aca aag gag gtg gtg tgc acc aac tgt cct act ggc acc act ggt   2304
Lys Thr Lys Glu Val Val Cys Thr Asn Cys Pro Thr Gly Thr Thr Gly
        755                 760                 765

aag aga tgt gag ctc tgt gat gat ggc tac ttt gga gac ccc ctg ggt   2352
Lys Arg Cys Glu Leu Cys Asp Asp Gly Tyr Phe Gly Asp Pro Leu Gly
    770                 775                 780

aga aac ggc cct gtg aga ctt tgc cgc ctg tgc cag tgc agt gac aac   2400
Arg Asn Gly Pro Val Arg Leu Cys Arg Leu Cys Gln Cys Ser Asp Asn
785                 790                 795                 800

atc gat ccc aac gca gtt gga aat tgc aat cgc ttg acg gga gaa tgc   2448
Ile Asp Pro Asn Ala Val Gly Asn Cys Asn Arg Leu Thr Gly Glu Cys
                805                 810                 815

ctg aag tgc atc tat aac act gct ggc ttc tat tgt gac cgg tgc aaa   2496
Leu Lys Cys Ile Tyr Asn Thr Ala Gly Phe Tyr Cys Asp Arg Cys Lys
            820                 825                 830

gac gga ttt ttt gga aat ccc ctg gct ccc aat cca gca gac aaa tgc   2544
Asp Gly Phe Phe Gly Asn Pro Leu Ala Pro Asn Pro Ala Asp Lys Cys
        835                 840                 845

aaa gcc tgc aat tgc aat ccg tat ggg acc atg aag cag cag agc agc   2592
Lys Ala Cys Asn Cys Asn Pro Tyr Gly Thr Met Lys Gln Gln Ser Ser
    850                 855                 860

tgt aac ccc gtg acg ggg cag tgt gaa tgt ttg cct cac gtg act ggc   2640
Cys Asn Pro Val Thr Gly Gln Cys Glu Cys Leu Pro His Val Thr Gly
865                 870                 875                 880
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cag gac tgt ggt gct tgt gac cct gga ttc tac aat ctg cag agt ggg   2688
Gln Asp Cys Gly Ala Cys Asp Pro Gly Phe Tyr Asn Leu Gln Ser Gly
                885                 890                 895

caa ggc tgt gag agg tgt gac tgc cat gcc ttg ggc tcc acc aat ggg   2736
Gln Gly Cys Glu Arg Cys Asp Cys His Ala Leu Gly Ser Thr Asn Gly
            900                 905                 910

cag tgt gac atc cgc acc ggc cag tgt gag tgc cag ccc ggc atc act   2784
Gln Cys Asp Ile Arg Thr Gly Gln Cys Glu Cys Gln Pro Gly Ile Thr
        915                 920                 925

ggt cag cac tgt gag cgc tgt gag gtc aac cac ttt ggg ttt gga cct   2832
Gly Gln His Cys Glu Arg Cys Glu Val Asn His Phe Gly Phe Gly Pro
    930                 935                 940

gaa ggc tgc aaa ccc tgt gac tgt cat cct gag gga tct ctt tca ctt   2880
Glu Gly Cys Lys Pro Cys Asp Cys His Pro Glu Gly Ser Leu Ser Leu
945                 950                 955                 960

cag tgc aaa gat gat ggt cgc tgt gaa tgc aga gaa ggc ttt gtg gga   2928
Gln Cys Lys Asp Asp Gly Arg Cys Glu Cys Arg Glu Gly Phe Val Gly
                965                 970                 975

aat cgc tgt gac cag tgt gaa gaa aac tat ttc tac aat cgg tct tgg   2976
Asn Arg Cys Asp Gln Cys Glu Glu Asn Tyr Phe Tyr Asn Arg Ser Trp
            980                 985                 990

cct ggc tgc cag gaa tgt cca gct tgt tac cgg ctg gta aag gat aag   3024
Pro Gly Cys Gln Glu Cys Pro Ala Cys Tyr Arg Leu Val Lys Asp Lys
        995                1000                1005

gtt gct gat cat aga gtg aag ctc cag gaa tta gag agt ctc ata gca   3072
Val Ala Asp His Arg Val Lys Leu Gln Glu Leu Glu Ser Leu Ile Ala
   1010                1015                1020

aac ctt gga act ggg gat gag atg gtg aca gat caa gcc ttc gag gat   3120
Asn Leu Gly Thr Gly Asp Glu Met Val Thr Asp Gln Ala Phe Glu Asp
1025                1030                1035                1040

aga cta aag gaa gca gag agg gaa gtt atg gac ctc ctt cgt gag gcc   3168
Arg Leu Lys Glu Ala Glu Arg Glu Val Met Asp Leu Leu Arg Glu Ala
                1045                1050                1055

cag gat gtc aaa gat gtt gac cag aat ttg atg gat cgc cta cag aga   3216
Gln Asp Val Lys Asp Val Asp Gln Asn Leu Met Asp Arg Leu Gln Arg
            1060                1065                1070

gtg aat aac act ctg tcc agc caa att agc cgt tta cag aat atc cgg   3264
Val Asn Asn Thr Leu Ser Ser Gln Ile Ser Arg Leu Gln Asn Ile Arg
        1075                1080                1085

aat acc att gaa gag act gga aac ttg gct gaa caa gcg cgt gcc cat   3312
Asn Thr Ile Glu Glu Thr Gly Asn Leu Ala Glu Gln Ala Arg Ala His
   1090                1095                1100

gta gag aac aca gag cgg ttg att gaa atc gca tcc aga gaa ctt gag   3360
Val Glu Asn Thr Glu Arg Leu Ile Glu Ile Ala Ser Arg Glu Leu Glu
1105                1110                1115                1120

aaa gca aaa gtc gct gct gcc aat gtg tca gtc act cag cca gaa tct   3408
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```
Lys Ala Lys Val Ala Ala Ala Asn Val Ser Val Thr Gln Pro Glu Ser
                1125                1130                1135

aca ggg gac cca aac aac atg act ctt ttg gca gaa gag gct cga aag   3456
Thr Gly Asp Pro Asn Asn Met Thr Leu Leu Ala Glu Glu Ala Arg Lys
            1140                1145                1150

ctt gct gaa cgt cat aaa cag gaa gct gat gac att gtt cga gtg gca   3504
Leu Ala Glu Arg His Lys Gln Glu Ala Asp Asp Ile Val Arg Val Ala
        1155                1160                1165

aag aca gcc aat gat acg tca act gag gca tac aac ctg ctt ctg agg   3552
Lys Thr Ala Asn Asp Thr Ser Thr Glu Ala Tyr Asn Leu Leu Leu Arg
    1170                1175                1180

aca ctg gca gga gaa aat caa aca gca ttt gag att gaa gag ctt aat   3600
Thr Leu Ala Gly Glu Asn Gln Thr Ala Phe Glu Ile Glu Glu Leu Asn
1185                1190                1195                1200

agg aag tat gaa caa gcg aag aac atc tca cag gat ctg gaa aaa caa   3648
Arg Lys Tyr Glu Gln Ala Lys Asn Ile Ser Gln Asp Leu Glu Lys Gln
                1205                1210                1215

gct gcc cga gta cat gag gag gcc aaa agg gcc ggt gac aaa gct gtg   3696
Ala Ala Arg Val His Glu Glu Ala Lys Arg Ala Gly Asp Lys Ala Val
            1220                1225                1230

gag atc tat gcc agc gtg gct cag ctg agc cct ttg gac tct gag aca   3744
Glu Ile Tyr Ala Ser Val Ala Gln Leu Ser Pro Leu Asp Ser Glu Thr
        1235                1240                1245

ctg gag aat gaa gca aat aac ata aag atg gaa gct gag aat ctg gaa   3792
Leu Glu Asn Glu Ala Asn Asn Ile Lys Met Glu Ala Glu Asn Leu Glu
    1250                1255                1260

caa ctg att gac cag aaa tta aaa gat tat gag gac ctc aga gaa gat   3840
Gln Leu Ile Asp Gln Lys Leu Lys Asp Tyr Glu Asp Leu Arg Glu Asp
1265                1270                1275                1280

atg aga ggg aag gaa ctt gaa gtc aag aac ctt ctg gag aaa ggc aag   3888
Met Arg Gly Lys Glu Leu Glu Val Lys Asn Leu Leu Glu Lys Gly Lys
                1285                1290                1295

act gaa cag cag acc gca gac caa ctc cta gcc cga gct gat gct gcc   3936
Thr Glu Gln Gln Thr Ala Asp Gln Leu Leu Ala Arg Ala Asp Ala Ala
            1300                1305                1310

aag gcc ctc gct gaa gaa gct gca aag aag gga cgg gat acc tta caa   3984
Lys Ala Leu Ala Glu Glu Ala Ala Lys Lys Gly Arg Asp Thr Leu Gln
        1315                1320                1325

gaa gct aat gac att ctc aac aac ctg aaa gat ttt gat agg cgc gtg   4032
Glu Ala Asn Asp Ile Leu Asn Asn Leu Lys Asp Phe Asp Arg Arg Val
    1330                1335                1340

aac gat aac aag acg gcc gca gag gag gca cta agg aag att cct gcc   4080
Asn Asp Asn Lys Thr Ala Ala Glu Glu Ala Leu Arg Lys Ile Pro Ala
1345                1350                1355                1360

atc aac cag acc atc act gaa gcc aat gaa aag acc aga gaa gcc cag   4128
Ile Asn Gln Thr Ile Thr Glu Ala Asn Glu Lys Thr Arg Glu Ala Gln
```

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                1365                1370                1375

cag gcc ctg ggc agt gct gcg gcg gat gcc aca gag gcc aag aac aag   4176
Gln Ala Leu Gly Ser Ala Ala Ala Asp Ala Thr Glu Ala Lys Asn Lys
          1380                1385                1390

gcc cat gag gcg gag agg atc gca agc gct gtc caa aag aat gcc acc   4224
Ala His Glu Ala Glu Arg Ile Ala Ser Ala Val Gln Lys Asn Ala Thr
       1395                1400                1405

agc acc aag gca gaa gct gaa aga act ttt gca gaa gtt aca gat ctg   4272
Ser Thr Lys Ala Glu Ala Glu Arg Thr Phe Ala Glu Val Thr Asp Leu
   1410                1415                1420

gat aat gag gtg aac aat atg ttg aag caa ctg cag gaa gca gaa aaa   4320
Asp Asn Glu Val Asn Asn Met Leu Lys Gln Leu Gln Glu Ala Glu Lys
1425                1430                1435                1440

gag cta aag aga aaa caa gat gac gct gac cag gac atg atg atg gca   4368
Glu Leu Lys Arg Lys Gln Asp Asp Ala Asp Gln Asp Met Met Met Ala
               1445                1450                1455

ggg atg gct tca cag gct gct caa gaa gcc gag atc aat gcc aga aaa   4416
Gly Met Ala Ser Gln Ala Ala Gln Glu Ala Glu Ile Asn Ala Arg Lys
          1460                1465                1470

gcc aaa aac tct gtt act agc ctc ctc agc att att aat gac ctc ttg   4464
Ala Lys Asn Ser Val Thr Ser Leu Leu Ser Ile Ile Asn Asp Leu Leu
       1475                1480                1485

gag cag ctg ggg cag ctg gat aca gtg gac ctg aat aag cta aac gag   4512
Glu Gln Leu Gly Gln Leu Asp Thr Val Asp Leu Asn Lys Leu Asn Glu
   1490                1495                1500

att gaa ggc acc cta aac aaa gcc aaa gat gaa atg aag gtc agc gat   4560
Ile Glu Gly Thr Leu Asn Lys Ala Lys Asp Glu Met Lys Val Ser Asp
1505                1510                1515                1520

ctt gat agg aaa gtg tct gac ctg gag aat gaa gcc aag aag cag gag   4608
Leu Asp Arg Lys Val Ser Asp Leu Glu Asn Glu Ala Lys Lys Gln Glu
               1525                1530                1535

gct gcc atc atg gac tat aac cga gat atc gag gag atc atg aag gac   4656
Ala Ala Ile Met Asp Tyr Asn Arg Asp Ile Glu Glu Ile Met Lys Asp
          1540                1545                1550

att cgc aat ctg gag gac atc agg aag acc tta cca tct ggc tgc ttc   4704
Ile Arg Asn Leu Glu Asp Ile Arg Lys Thr Leu Pro Ser Gly Cys Phe
       1555                1560                1565

aac acc ccg tcc att gaa aag ccc tagtgtcttt agggctggaa ggcagcatcc  4758
Asn Thr Pro Ser Ile Glu Lys Pro
   1570                1575

ctctgacagg ggggcagttg tgaggccaca gagtgccttg acacaaagat tacatttttc 4818

agacccccac tcctctgctg ctgtccatca ctgtcctttt gaaccaggaa aagtcacaga 4878

gtttaaagag aagcaaatta aacatcctga atcgggaaca aagggtttta tctaataaag 4938

tgtctcttcc                                                        4948
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<213> Homo sapiens

<400> 24

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Cys Met Pro Glu Phe Val Asn Ala Ala Phe Asn Val Thr Val Val Ala
            20                  25                  30

Thr Asn Thr Cys Gly Thr Pro Pro Glu Glu Tyr Cys Val Gln Thr Gly
        35                  40                  45

Val Thr Gly Val Thr Lys Ser Cys His Leu Cys Asp Ala Gly Gln Pro
    50                  55                  60

His Leu Gln His Gly Ala Ala Phe Leu Thr Asp Tyr Asn Asn Gln Ala
65                  70                  75                  80

Asp Thr Thr Trp Trp Gln Ser Gln Thr Met Leu Ala Gly Val Gln Tyr
                85                  90                  95

Pro Ser Ser Ile Asn Leu Thr Leu His Leu Gly Lys Ala Phe Asp Ile
            100                 105                 110

Thr Tyr Val Arg Leu Lys Phe His Thr Ser Arg Pro Glu Ser Phe Ala
        115                 120                 125

Ile Tyr Lys Arg Thr Arg Glu Asp Gly Pro Trp Ile Pro Tyr Gln Tyr
    130                 135                 140

Tyr Ser Gly Ser Cys Glu Asn Thr Tyr Ser Lys Ala Asn Arg Gly Phe
145                 150                 155                 160

Ile Arg Thr Gly Gly Asp Glu Gln Gln Ala Leu Cys Thr Asp Glu Phe
                165                 170                 175

Ser Asp Ile Ser Pro Leu Thr Gly Gly Asn Val Ala Phe Ser Thr Leu
            180                 185                 190

Glu Gly Arg Pro Ser Ala Tyr Asn Phe Asp Asn Ser Pro Val Leu Gln
        195                 200                 205

Glu Trp Val Thr Ala Thr Asp Ile Arg Val Thr Leu Asn Arg Leu Asn
    210                 215                 220

Thr Phe Gly Asp Glu Val Phe Asn Asp Pro Lys Val Leu Lys Ser Tyr
225                 230                 235                 240

Tyr Tyr Ala Ile Ser Asp Phe Ala Val Gly Gly Arg Cys Lys Cys Asn
                245                 250                 255

Gly His Ala Ser Glu Cys Met Lys Asn Glu Phe Asp Lys Leu Val Cys
            260                 265                 270

Asn Cys Lys His Asn Thr Tyr Gly Val Asp Cys Glu Lys Cys Leu Pro
        275                 280                 285
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Phe Phe Asn Asp Arg Pro Trp Arg Arg Ala Thr Ala Glu Ser Ala Ser
    290                 295                 300

Glu Cys Leu Pro Cys Asp Cys Asn Gly Arg Ser Gln Glu Cys Tyr Phe
305                 310                 315                 320

Asp Pro Glu Leu Tyr Arg Ser Thr Gly His Gly Gly His Cys Thr Asn
                325                 330                 335

Cys Gln Asp Asn Thr Asp Gly Ala His Cys Glu Arg Cys Arg Glu Asn
            340                 345                 350

Phe Phe Arg Leu Gly Asn Asn Glu Ala Cys Ser Ser Cys His Cys Ser
        355                 360                 365

Pro Val Gly Ser Leu Ser Thr Gln Cys Asp Ser Tyr Gly Arg Cys Ser
    370                 375                 380

Cys Lys Pro Gly Val Met Gly Asp Lys Cys Asp Arg Cys Gln Pro Gly
385                 390                 395                 400

Phe His Ser Leu Thr Glu Ala Gly Cys Arg Pro Cys Ser Cys Asp Pro
                405                 410                 415

Ser Gly Ser Ile Asp Glu Cys Asn Val Glu Thr Gly Arg Cys Val Cys
            420                 425                 430

Lys Asp Asn Val Glu Gly Phe Asn Cys Glu Arg Cys Lys Pro Gly Phe
        435                 440                 445

Phe Asn Leu Glu Ser Ser Asn Pro Arg Gly Cys Thr Pro Cys Phe Cys
    450                 455                 460

Phe Gly His Ser Ser Val Cys Thr Asn Ala Val Gly Tyr Ser Val Tyr
465                 470                 475                 480

Ser Ile Ser Ser Thr Phe Gln Ile Asp Glu Asp Gly Trp Arg Ala Glu
                485                 490                 495

Gln Arg Asp Gly Ser Glu Ala Ser Leu Glu Trp Ser Ser Glu Arg Gln
            500                 505                 510

Asp Ile Ala Val Ile Ser Asp Ser Tyr Phe Pro Arg Tyr Phe Ile Ala
        515                 520                 525

Pro Ala Lys Phe Leu Gly Lys Gln Val Leu Ser Tyr Gly Gln Asn Leu
    530                 535                 540

Ser Phe Ser Phe Arg Val Asp Arg Arg Asp Thr Arg Leu Ser Ala Glu
545                 550                 555                 560

Asp Leu Val Leu Glu Gly Ala Gly Leu Arg Val Ser Val Pro Leu Ile
                565                 570                 575

Ala Gln Gly Asn Ser Tyr Pro Ser Glu Thr Thr Val Lys Tyr Val Phe
            580                 585                 590

Arg Leu His Glu Ala Thr Asp Tyr Pro Trp Arg Pro Ala Leu Thr Pro
        595                 600                 605
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Phe Glu Phe Gln Lys Leu Leu Asn Asn Leu Thr Ser Ile Lys Ile Arg
    610                 615                 620

Gly Thr Tyr Ser Glu Arg Ser Ala Gly Tyr Leu Asp Asp Val Thr Leu
625                 630                 635                 640

Ala Ser Ala Arg Pro Gly Pro Gly Val Pro Ala Thr Trp Val Glu Ser
                645                 650                 655

Cys Thr Cys Pro Val Gly Tyr Gly Gly Gln Phe Cys Glu Met Cys Leu
            660                 665                 670

Ser Gly Tyr Arg Arg Glu Thr Pro Asn Leu Gly Pro Tyr Ser Pro Cys
        675                 680                 685

Val Leu Cys Ala Cys Asn Gly His Ser Glu Thr Cys Asp Pro Glu Thr
    690                 695                 700

Gly Val Cys Asn Cys Arg Asp Asn Thr Ala Gly Pro His Cys Glu Lys
705                 710                 715                 720

Cys Ser Asp Gly Tyr Tyr Gly Asp Ser Thr Ala Gly Thr Ser Ser Asp
                725                 730                 735

Cys Gln Pro Cys Pro Cys Pro Gly Gly Ser Ser Cys Ala Val Val Pro
            740                 745                 750

Lys Thr Lys Glu Val Val Cys Thr Asn Cys Pro Thr Gly Thr Thr Gly
        755                 760                 765

Lys Arg Cys Glu Leu Cys Asp Asp Gly Tyr Phe Gly Asp Pro Leu Gly
    770                 775                 780

Arg Asn Gly Pro Val Arg Leu Cys Arg Leu Cys Gln Cys Ser Asp Asn
785                 790                 795                 800

Ile Asp Pro Asn Ala Val Gly Asn Cys Asn Arg Leu Thr Gly Glu Cys
                805                 810                 815

Leu Lys Cys Ile Tyr Asn Thr Ala Gly Phe Tyr Cys Asp Arg Cys Lys
            820                 825                 830

Asp Gly Phe Phe Gly Asn Pro Leu Ala Pro Asn Pro Ala Asp Lys Cys
        835                 840                 845

Lys Ala Cys Asn Cys Asn Pro Tyr Gly Thr Met Lys Gln Gln Ser Ser
    850                 855                 860

Cys Asn Pro Val Thr Gly Gln Cys Glu Cys Leu Pro His Val Thr Gly
865                 870                 875                 880

Gln Asp Cys Gly Ala Cys Asp Pro Gly Phe Tyr Asn Leu Gln Ser Gly
                885                 890                 895

Gln Gly Cys Glu Arg Cys Asp Cys His Ala Leu Gly Ser Thr Asn Gly
            900                 905                 910

Gln Cys Asp Ile Arg Thr Gly Gln Cys Glu Cys Gln Pro Gly Ile Thr
        915                 920                 925

Gly Gln His Cys Glu Arg Cys Glu Val Asn His Phe Gly Phe Gly Pro
```

930 935 940

Glu Gly Cys Lys Pro Cys Asp Cys His Pro Glu Gly Ser Leu Ser Leu
945 950 955 960

Gln Cys Lys Asp Asp Gly Arg Cys Glu Cys Arg Glu Gly Phe Val Gly
965 970 975

Asn Arg Cys Asp Gln Cys Glu Glu Asn Tyr Phe Tyr Asn Arg Ser Trp
980 985 990

Pro Gly Cys Gln Glu Cys Pro Ala Cys Tyr Arg Leu Val Lys Asp Lys
995 1000 1005

Val Ala Asp His Arg Val Lys Leu Gln Glu Leu Glu Ser Leu Ile Ala
1010 1015 1020

Asn Leu Gly Thr Gly Asp Glu Met Val Thr Asp Gln Ala Phe Glu Asp
1025 1030 1035 1040

Arg Leu Lys Glu Ala Glu Arg Glu Val Met Asp Leu Leu Arg Glu Ala
1045 1050 1055

Gln Asp Val Lys Asp Val Asp Gln Asn Leu Met Asp Arg Leu Gln Arg
1060 1065 1070

Val Asn Asn Thr Leu Ser Ser Gln Ile Ser Arg Leu Gln Asn Ile Arg
1075 1080 1085

Asn Thr Ile Glu Glu Thr Gly Asn Leu Ala Glu Gln Ala Arg Ala His
1090 1095 1100

Val Glu Asn Thr Glu Arg Leu Ile Glu Ile Ala Ser Arg Glu Leu Glu
1105 1110 1115 1120

Lys Ala Lys Val Ala Ala Ala Asn Val Ser Val Thr Gln Pro Glu Ser
1125 1130 1135

Thr Gly Asp Pro Asn Asn Met Thr Leu Leu Ala Glu Glu Ala Arg Lys
1140 1145 1150

Leu Ala Glu Arg His Lys Gln Glu Ala Asp Asp Ile Val Arg Val Ala
1155 1160 1165

Lys Thr Ala Asn Asp Thr Ser Thr Glu Ala Tyr Asn Leu Leu Leu Arg
1170 1175 1180

Thr Leu Ala Gly Glu Asn Gln Thr Ala Phe Glu Ile Glu Glu Leu Asn
1185 1190 1195 1200

Arg Lys Tyr Glu Gln Ala Lys Asn Ile Ser Gln Asp Leu Glu Lys Gln
1205 1210 1215

Ala Ala Arg Val His Glu Glu Ala Lys Arg Ala Gly Asp Lys Ala Val
1220 1225 1230

Glu Ile Tyr Ala Ser Val Ala Gln Leu Ser Pro Leu Asp Ser Glu Thr
1235 1240 1245

Leu Glu Asn Glu Ala Asn Asn Ile Lys Met Glu Ala Glu Asn Leu Glu
1250 1255 1260

Gln Leu Ile Asp Gln Lys Leu Lys Asp Tyr Glu Asp Leu Arg Glu Asp
1265 1270 1275 1280

Met Arg Gly Lys Glu Leu Glu Val Lys Asn Leu Leu Glu Lys Gly Lys
1285 1290 1295

Thr Glu Gln Gln Thr Ala Asp Gln Leu Leu Ala Arg Ala Asp Ala Ala
1300 1305 1310

Lys Ala Leu Ala Glu Glu Ala Ala Lys Lys Gly Arg Asp Thr Leu Gln
1315 1320 1325

Glu Ala Asn Asp Ile Leu Asn Asn Leu Lys Asp Phe Asp Arg Arg Val
1330 1335 1340

Asn Asp Asn Lys Thr Ala Ala Glu Glu Ala Leu Arg Lys Ile Pro Ala
1345 1350 1355 1360

Ile Asn Gln Thr Ile Thr Glu Ala Asn Glu Lys Thr Arg Glu Ala Gln
1365 1370 1375

Gln Ala Leu Gly Ser Ala Ala Ala Asp Ala Thr Glu Ala Lys Asn Lys
1380 1385 1390

Ala His Glu Ala Glu Arg Ile Ala Ser Ala Val Gln Lys Asn Ala Thr
1395 1400 1405

Ser Thr Lys Ala Glu Ala Glu Arg Thr Phe Ala Glu Val Thr Asp Leu
1410 1415 1420

Asp Asn Glu Val Asn Asn Met Leu Lys Gln Leu Gln Glu Ala Glu Lys
1425 1430 1435 1440

Glu Leu Lys Arg Lys Gln Asp Asp Ala Asp Gln Asp Met Met Met Ala
1445 1450 1455

Gly Met Ala Ser Gln Ala Ala Gln Glu Ala Glu Ile Asn Ala Arg Lys
1460 1465 1470

Ala Lys Asn Ser Val Thr Ser Leu Leu Ser Ile Ile Asn Asp Leu Leu
1475 1480 1485

Glu Gln Leu Gly Gln Leu Asp Thr Val Asp Leu Asn Lys Leu Asn Glu
1490 1495 1500

Ile Glu Gly Thr Leu Asn Lys Ala Lys Asp Glu Met Lys Val Ser Asp
1505 1510 1515 1520

Leu Asp Arg Lys Val Ser Asp Leu Glu Asn Glu Ala Lys Lys Gln Glu
1525 1530 1535

Ala Ala Ile Met Asp Tyr Asn Arg Asp Ile Glu Glu Ile Met Lys Asp
1540 1545 1550

Ile Arg Asn Leu Glu Asp Ile Arg Lys Thr Leu Pro Ser Gly Cys Phe
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Asn Thr Pro Ser Ile Glu Lys Pro
1570 1575

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ggcctcggga tacgccgcta ggcgagtgca gcgcggcacc ccagcctttg ccgaggggcc 180

cgccgcagcg gg atg acg ggc ggc ggg cgg gcc gcg ctg gcc ctg cag ccc 231
Met Thr Gly Gly Gly Arg Ala Ala Leu Ala Leu Gln Pro
1 5 10

cgg ggg cgg ctg tgg ccg ctg ttg gct gtg ctg gcg gct gtg gcg ggc 279
Arg Gly Arg Leu Trp Pro Leu Leu Ala Val Leu Ala Ala Val Ala Gly
15 20 25

tgt gtc cgg gcg gcc atg gac gag tgc gcg gat gag ggc ggg cgg ccg 327
Cys Val Arg Ala Ala Met Asp Glu Cys Ala Asp Glu Gly Gly Arg Pro
30 35 40 45

cag cgc tgc atg ccg gag ttt gtt aat gcc gcc ttc aat gtg acc gtg 375
Gln Arg Cys Met Pro Glu Phe Val Asn Ala Ala Phe Asn Val Thr Val
50 55 60

gtg gct acc aac acg tgt ggg act ccg ccc gag gag tac tgc gtg cag 423
Val Ala Thr Asn Thr Cys Gly Thr Pro Pro Glu Glu Tyr Cys Val Gln
65 70 75

act ggg gtg acc gga gtc act aag tcc tgt cac ctg tgc gac gcc ggc 471
Thr Gly Val Thr Gly Val Thr Lys Ser Cys His Leu Cys Asp Ala Gly
80 85 90

cag cag cac ctg caa cac ggg gca gcc ttc ctg acc gac tac aac aac 519
Gln Gln His Leu Gln His Gly Ala Ala Phe Leu Thr Asp Tyr Asn Asn
95 100 105

cag gcc gac acc acc tgg tgg caa agc cag act atg ctg gcc ggg gtg 567
Gln Ala Asp Thr Thr Trp Trp Gln Ser Gln Thr Met Leu Ala Gly Val
110 115 120 125

cag tac ccc aac tcc atc aac ctc acg ctg cac ctg gga aag gct ttt 615
Gln Tyr Pro Asn Ser Ile Asn Leu Thr Leu His Leu Gly Lys Ala Phe
130 135 140

gac atc act tac gtg cgc ctc aag ttc cac acc agc cgt cca gag agc 663
Asp Ile Thr Tyr Val Arg Leu Lys Phe His Thr Ser Arg Pro Glu Ser
145 150 155

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ttc gcc atc tat aag cgc act cgg gaa gac ggg ccc tgg att cct tat   711
Phe Ala Ile Tyr Lys Arg Thr Arg Glu Asp Gly Pro Trp Ile Pro Tyr
        160                 165                 170

cag tac tac agt ggg tcc tgt gag aac acg tac tca aag gct aac cgt   759
Gln Tyr Tyr Ser Gly Ser Cys Glu Asn Thr Tyr Ser Lys Ala Asn Arg
    175                 180                 185

ggc ttc atc agg acc gga ggg gac gag cag cag gcc ttg tgt act gat   807
Gly Phe Ile Arg Thr Gly Gly Asp Glu Gln Gln Ala Leu Cys Thr Asp
190                 195                 200                 205

gaa ttc agt gac att tcc ccc ctc acc ggt ggc aac gtg gcc ttt tca   855
Glu Phe Ser Asp Ile Ser Pro Leu Thr Gly Gly Asn Val Ala Phe Ser
                210                 215                 220

acc ctg gaa gga cgg ccg agt gcc tac aac ttt gac aac agc cct gtg   903
Thr Leu Glu Gly Arg Pro Ser Ala Tyr Asn Phe Asp Asn Ser Pro Val
            225                 230                 235

ctc cag gaa tgg gta act gcc act gac atc aga gtg acg ctc aat cgc   951
Leu Gln Glu Trp Val Thr Ala Thr Asp Ile Arg Val Thr Leu Asn Arg
        240                 245                 250

ctg aac acc ttt gga gat gaa gtg ttt aac gac ccc aaa gtt ctc aag   999
Leu Asn Thr Phe Gly Asp Glu Val Phe Asn Asp Pro Lys Val Leu Lys
    255                 260                 265

tct tac tat tac gca atc tca gac ttt gct gtg ggc ggc agg tgt aaa  1047
Ser Tyr Tyr Tyr Ala Ile Ser Asp Phe Ala Val Gly Gly Arg Cys Lys
270                 275                 280                 285

tgt aac gga cat gcc agc gag tgt gta aag aac gag ttt gac aaa ctc  1095
Cys Asn Gly His Ala Ser Glu Cys Val Lys Asn Glu Phe Asp Lys Leu
                290                 295                 300

atg tgc aac tgc aaa cat aac aca tac gga gtt gac tgt gaa aag tgc  1143
Met Cys Asn Cys Lys His Asn Thr Tyr Gly Val Asp Cys Glu Lys Cys
            305                 310                 315

ctg cct ttc ttc aat gac cgg ccg tgg agg agg gcg act gct gag agc  1191
Leu Pro Phe Phe Asn Asp Arg Pro Trp Arg Arg Ala Thr Ala Glu Ser
        320                 325                 330

gcc agc gag tgc ctt cct tgt gac tgc aat ggc cga tcc caa gag tgc  1239
Ala Ser Glu Cys Leu Pro Cys Asp Cys Asn Gly Arg Ser Gln Glu Cys
    335                 340                 345

tac ttt gat cct gaa cta tac cgt tcc act gga cat ggt ggc cac tgt  1287
Tyr Phe Asp Pro Glu Leu Tyr Arg Ser Thr Gly His Gly Gly His Cys
350                 355                 360                 365

acc aac tgc cgg gat aac aca gat ggt gcc aag tgc gag agg tgc cgg  1335
Thr Asn Cys Arg Asp Asn Thr Asp Gly Ala Lys Cys Glu Arg Cys Arg
                370                 375                 380

gag aat ttc ttc cgc ctg ggg aac act gaa gcc tgc tct ccg tgc cac  1383
Glu Asn Phe Phe Arg Leu Gly Asn Thr Glu Ala Cys Ser Pro Cys His
            385                 390                 395

tgc agc cct gtt ggt tct ctc agc aca cag tgt gac agt tac ggc aga  1431
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Cys Ser Pro Val Gly Ser Leu Ser Thr Gln Cys Asp Ser Tyr Gly Arg
        400                 405                 410

tgc agc tgt aag cca gga gtg atg ggt gac aag tgt gac cgt tgt cag   1479
Cys Ser Cys Lys Pro Gly Val Met Gly Asp Lys Cys Asp Arg Cys Gln
    415                 420                 425

cct ggg ttc cat tcc ctc act gag gca gga tgc agg cca tgc tcc tgc   1527
Pro Gly Phe His Ser Leu Thr Glu Ala Gly Cys Arg Pro Cys Ser Cys
430                 435                 440                 445

gat cct tcg ggc agc aca gac gag tgt aat gtt gaa aca gga aga tgc   1575
Asp Pro Ser Gly Ser Thr Asp Glu Cys Asn Val Glu Thr Gly Arg Cys
                450                 455                 460

gtt tgc aaa gac aat gtt gaa ggc ttc aac tgt gag aga tgc aaa cct   1623
Val Cys Lys Asp Asn Val Glu Gly Phe Asn Cys Glu Arg Cys Lys Pro
            465                 470                 475

gga ttt ttt aat ctg gag tca tct aat cct aag ggc tgc aca ccc tgc   1671
Gly Phe Phe Asn Leu Glu Ser Ser Asn Pro Lys Gly Cys Thr Pro Cys
        480                 485                 490

ttc tgc ttt ggc cat tct tct gtg tgc aca aat gct gtt ggc tac agt   1719
Phe Cys Phe Gly His Ser Ser Val Cys Thr Asn Ala Val Gly Tyr Ser
    495                 500                 505

gtt tat gac atc tcc tcc acc ttt cag att gat gag gat ggg tgg cgc   1767
Val Tyr Asp Ile Ser Ser Thr Phe Gln Ile Asp Glu Asp Gly Trp Arg
510                 515                 520                 525

gtg gag cag aga gat ggc tcg gag gcg tct ctg gag tgg tcc tca gac   1815
Val Glu Gln Arg Asp Gly Ser Glu Ala Ser Leu Glu Trp Ser Ser Asp
                530                 535                 540

agg caa tat att gcc gta atc tca gac agt tac ttt cct aga tac ttc   1863
Arg Gln Tyr Ile Ala Val Ile Ser Asp Ser Tyr Phe Pro Arg Tyr Phe
            545                 550                 555

atc gcc cct gtg aag ttc ctg ggc aac cag gtc ctg agt tat ggg cag   1911
Ile Ala Pro Val Lys Phe Leu Gly Asn Gln Val Leu Ser Tyr Gly Gln
        560                 565                 570

aat ctt tcc ttc tcc ttc cga gtg gac aga cga gac act cgc ctc tcc   1959
Asn Leu Ser Phe Ser Phe Arg Val Asp Arg Arg Asp Thr Arg Leu Ser
    575                 580                 585

gca gag gac ctt gtg ctc gaa gga gct ggc ttg aga gta tcc gtg ccc   2007
Ala Glu Asp Leu Val Leu Glu Gly Ala Gly Leu Arg Val Ser Val Pro
590                 595                 600                 605

ttg atc gct cag ggc aac tcc tac ccc agc gag acc act gtg aag tac   2055
Leu Ile Ala Gln Gly Asn Ser Tyr Pro Ser Glu Thr Thr Val Lys Tyr
                610                 615                 620

atc ttc agg ctc cat gaa gca acg gat tac cct tgg agg ccc gct ctc   2103
Ile Phe Arg Leu His Glu Ala Thr Asp Tyr Pro Trp Arg Pro Ala Leu
            625                 630                 635

tcc ccg ttt gaa ttt cag aag ctc ctg aac aac ttg acc tct atc aag   2151
Ser Pro Phe Glu Phe Gln Lys Leu Leu Asn Asn Leu Thr Ser Ile Lys
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        640                 645                 650

atc cgt ggt aca tac agc gag agg agc gct ggg tac ttg gat gat gtc   2199
Ile Arg Gly Thr Tyr Ser Glu Arg Ser Ala Gly Tyr Leu Asp Asp Val
    655                 660                 665

acc ttg caa agt gct cgc cct ggg ccc gga gtc cct gca acg tgg gtg   2247
Thr Leu Gln Ser Ala Arg Pro Gly Pro Gly Val Pro Ala Thr Trp Val
670                 675                 680                 685

gag tcc tgc acc tgt cca gtg gga tac ggg gga cag ttc tgt gag acg   2295
Glu Ser Cys Thr Cys Pro Val Gly Tyr Gly Gly Gln Phe Cys Glu Thr
                690                 695                 700

tgc ctc cca ggg tac aga aga gaa act cca agc ctt gga cct tat agc   2343
Cys Leu Pro Gly Tyr Arg Arg Glu Thr Pro Ser Leu Gly Pro Tyr Ser
            705                 710                 715

ccg tgt gtg ctc tgt acc tgt aat ggg cac agt gag acc tgt gac ccg   2391
Pro Cys Val Leu Cys Thr Cys Asn Gly His Ser Glu Thr Cys Asp Pro
        720                 725                 730

gag aca ggt gtc tgt gac tgc aga gac aat aca gcc ggc ccc cac tgt   2439
Glu Thr Gly Val Cys Asp Cys Arg Asp Asn Thr Ala Gly Pro His Cys
    735                 740                 745

gag aaa tgt agc gat ggg tac tat ggg gac tca acc ctg ggc acc tcc   2487
Glu Lys Cys Ser Asp Gly Tyr Tyr Gly Asp Ser Thr Leu Gly Thr Ser
750                 755                 760                 765

tct gac tgc cag cct tgt ccc tgc ccc ggt ggc tca agt tgt gcc att   2535
Ser Asp Cys Gln Pro Cys Pro Cys Pro Gly Gly Ser Ser Cys Ala Ile
                770                 775                 780

gtc cca aag aca aag gaa gtg gtg tgc acg cac tgt ccg act ggc act   2583
Val Pro Lys Thr Lys Glu Val Val Cys Thr His Cys Pro Thr Gly Thr
            785                 790                 795

gcc ggc aag aga tgt gaa ctc tgt gat gac ggc tac ttt gga gac cct   2631
Ala Gly Lys Arg Cys Glu Leu Cys Asp Asp Gly Tyr Phe Gly Asp Pro
        800                 805                 810

ctg ggc agc aat ggg ccc gtg aga ctg tgc cgc ccg tgc cag tgt aac   2679
Leu Gly Ser Asn Gly Pro Val Arg Leu Cys Arg Pro Cys Gln Cys Asn
    815                 820                 825

gac aac ata gac ccc aac gcg gtt ggc aac tgc aac cgc ctg acg ggc   2727
Asp Asn Ile Asp Pro Asn Ala Val Gly Asn Cys Asn Arg Leu Thr Gly
830                 835                 840                 845

gag tgc ctg aag tgc atc tat aac acg gct ggt ttc tac tgc gac cgg   2775
Glu Cys Leu Lys Cys Ile Tyr Asn Thr Ala Gly Phe Tyr Cys Asp Arg
                850                 855                 860

tgc aag gaa ggg ttt ttc gga aat ccc ctg gct ccc aat cca gcc gac   2823
Cys Lys Glu Gly Phe Phe Gly Asn Pro Leu Ala Pro Asn Pro Ala Asp
            865                 870                 875

aaa tgc aaa gcc tgc gcc tgc aac tac ggg aca gtg cag caa cag agc   2871
Lys Cys Lys Ala Cys Ala Cys Asn Tyr Gly Thr Val Gln Gln Gln Ser
        880                 885                 890
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agc tgt aac ccg gtg acc gga caa tgc cag tgt ctg cct cat gtg tct   2919
Ser Cys Asn Pro Val Thr Gly Gln Cys Gln Cys Leu Pro His Val Ser
    895                 900                 905

ggc cgc gac tgc ggt act tgt gac cct ggc tac tac aac ctg cag agc   2967
Gly Arg Asp Cys Gly Thr Cys Asp Pro Gly Tyr Tyr Asn Leu Gln Ser
910                 915                 920                 925

ggg caa ggc tgc gag agg tgt gac tgc cat gct ttg ggt tcc acc aat   3015
Gly Gln Gly Cys Glu Arg Cys Asp Cys His Ala Leu Gly Ser Thr Asn
                930                 935                 940

ggg cag tgt gac atc cgc acc ggg cag tgt gag tgc cag cct ggc atc   3063
Gly Gln Cys Asp Ile Arg Thr Gly Gln Cys Glu Cys Gln Pro Gly Ile
            945                 950                 955

acc ggt cag cac tgt gag cgc tgt gag acc aac cac ttt ggg ttt gga   3111
Thr Gly Gln His Cys Glu Arg Cys Glu Thr Asn His Phe Gly Phe Gly
        960                 965                 970

cct gaa ggc tgc aaa cct tgt gac tgt cac cat gaa gga tcc ctt tcg   3159
Pro Glu Gly Cys Lys Pro Cys Asp Cys His His Glu Gly Ser Leu Ser
    975                 980                 985

ctc cag tgt aaa gac gac ggc cgt tgt gaa tgc agg gaa ggc ttt gtg   3207
Leu Gln Cys Lys Asp Asp Gly Arg Cys Glu Cys Arg Glu Gly Phe Val
990                 995                1000                1005

ggc aat cgc tgt gac cag tgt gaa gag aac tat ttc tac aat cgg tcc   3255
Gly Asn Arg Cys Asp Gln Cys Glu Glu Asn Tyr Phe Tyr Asn Arg Ser
               1010                1015                1020

tgg cct ggc tgc cag gag tgt ccg gct tgt tac cga ctt gtg aag gat   3303
Trp Pro Gly Cys Gln Glu Cys Pro Ala Cys Tyr Arg Leu Val Lys Asp
          1025                1030                1035

aag gct gct gag cat cga gtg aaa ctc cag gag tta gag agc ctc atc   3351
Lys Ala Ala Glu His Arg Val Lys Leu Gln Glu Leu Glu Ser Leu Ile
      1040                1045                1050

gcc aac ctt ggc act ggg gat gac atg gtg aca gat caa gcc ttt gag   3399
Ala Asn Leu Gly Thr Gly Asp Asp Met Val Thr Asp Gln Ala Phe Glu
  1055                1060                1065

gac aga ctt aag gaa gca gaa agg gag gtg aca gac ctt ctc cgt gag   3447
Asp Arg Leu Lys Glu Ala Glu Arg Glu Val Thr Asp Leu Leu Arg Glu
1070                1075                1080                1085

gct cag gaa gtc aaa gat gta gat caa aat ctg atg gat cgc ctt cag   3495
Ala Gln Glu Val Lys Asp Val Asp Gln Asn Leu Met Asp Arg Leu Gln
               1090                1095                1100

aga gta aat agc agc ctg cat agc caa att agc cga ctg cag aat atc   3543
Arg Val Asn Ser Ser Leu His Ser Gln Ile Ser Arg Leu Gln Asn Ile
          1105                1110                1115

cgg aat act atc gaa gag acc ggg atc ttg gct gag cga gca cgg tcc   3591
Arg Asn Thr Ile Glu Glu Thr Gly Ile Leu Ala Glu Arg Ala Arg Ser
      1120                1125                1130
```

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cga gtg gag agt aca gag cag ctg att gag atc gcc tcc agg gag ctc   3639
Arg Val Glu Ser Thr Glu Gln Leu Ile Glu Ile Ala Ser Arg Glu Leu
   1135                1140                1145

gag aaa gca aaa atg gcc gcc aat gtg tca atc act cag cca gag tct   3687
Glu Lys Ala Lys Met Ala Ala Asn Val Ser Ile Thr Gln Pro Glu Ser
1150                1155                1160                1165

aca ggg gag cca aac aac atg acc ctc ttg gca gaa gaa gcc cga agg   3735
Thr Gly Glu Pro Asn Asn Met Thr Leu Leu Ala Glu Glu Ala Arg Arg
               1170                1175                1180

ctt gca gag cgt cat aaa cag gaa gcc gat gac att gta cga gtg gca   3783
Leu Ala Glu Arg His Lys Gln Glu Ala Asp Asp Ile Val Arg Val Ala
          1185                1190                1195

aag aca gcc aac gag act tca gct gag gca tat aat ctg ctt ttg agg   3831
Lys Thr Ala Asn Glu Thr Ser Ala Glu Ala Tyr Asn Leu Leu Leu Arg
       1200                1205                1210

acc ctg gca gga gaa aat caa act gcg ctg gag att gaa gaa ctt aac   3879
Thr Leu Ala Gly Glu Asn Gln Thr Ala Leu Glu Ile Glu Glu Leu Asn
   1215                1220                1225

cgg aag tac gaa caa gca aag aac atc tct cag gac ctg gag aag cag   3927
Arg Lys Tyr Glu Gln Ala Lys Asn Ile Ser Gln Asp Leu Glu Lys Gln
1230                1235                1240                1245

gct gcc cga gtc cat gag gaa gcc aag cgt gca ggt gac aaa gcc gta   3975
Ala Ala Arg Val His Glu Glu Ala Lys Arg Ala Gly Asp Lys Ala Val
               1250                1255                1260

gag atc tat gcc agt gtg gcc cag ctg acc cct gtg gac tct gag gcc   4023
Glu Ile Tyr Ala Ser Val Ala Gln Leu Thr Pro Val Asp Ser Glu Ala
          1265                1270                1275

ctg gag aat gaa gca aat aaa atc aag aaa gaa gct gca gac ctg gac   4071
Leu Glu Asn Glu Ala Asn Lys Ile Lys Lys Glu Ala Ala Asp Leu Asp
       1280                1285                1290

cgt ctg att gac cag aag cta aag gat tac gag gac ctc agg gaa gac   4119
Arg Leu Ile Asp Gln Lys Leu Lys Asp Tyr Glu Asp Leu Arg Glu Asp
   1295                1300                1305

atg aga gga aag gaa cat gaa gtg aag aac ctt cta gag aag ggg aaa   4167
Met Arg Gly Lys Glu His Glu Val Lys Asn Leu Leu Glu Lys Gly Lys
1310                1315                1320                1325

gct gaa cag cag acc gcc gac caa ctc cta gct cga gcc gat gct gcc   4215
Ala Glu Gln Gln Thr Ala Asp Gln Leu Leu Ala Arg Ala Asp Ala Ala
               1330                1335                1340

aag gcc ctt gct gaa gaa gct gct aag aag gga cgc agt acc tta caa   4263
Lys Ala Leu Ala Glu Glu Ala Ala Lys Lys Gly Arg Ser Thr Leu Gln
          1345                1350                1355

gaa gcc aat gac att ctc aac aac ctg aaa gat ttt gat aga cgt gtg   4311
Glu Ala Asn Asp Ile Leu Asn Asn Leu Lys Asp Phe Asp Arg Arg Val
       1360                1365                1370

aac gat aac aag aca gcc gcg gaa gaa gct cta agg aga att ccc gcc   4359
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Asn Asp Asn Lys Thr Ala Ala Glu Glu Ala Leu Arg Arg Ile Pro Ala
   1375                1380                1385

atc aac cgg acc ata gct gaa gcc aat gag aag aca agg gag gcc cag   4407
Ile Asn Arg Thr Ile Ala Glu Ala Asn Glu Lys Thr Arg Glu Ala Gln
1390               1395                1400                1405

cta gcg ctg ggc aat gct gcc gct gac gcc acg gag gcc aag aac aag   4455
Leu Ala Leu Gly Asn Ala Ala Ala Asp Ala Thr Glu Ala Lys Asn Lys
               1410                1415                1420

gcc cat gag gca gag agg atc gcc agc gcc gcg cag aag aat gcc acc   4503
Ala His Glu Ala Glu Arg Ile Ala Ser Ala Ala Gln Lys Asn Ala Thr
          1425                1430                1435

agt acc aag gcg gac gca gaa aga acc ttc ggg gaa gtt aca gat ctg   4551
Ser Thr Lys Ala Asp Ala Glu Arg Thr Phe Gly Glu Val Thr Asp Leu
       1440                1445                1450

gat aat gag gtg aac ggt atg ctg agg cag cta gag gag gca gag aat   4599
Asp Asn Glu Val Asn Gly Met Leu Arg Gln Leu Glu Glu Ala Glu Asn
   1455                1460                1465

gag ctg aag agg aag caa gat gac gcc gac cag gac atg atg atg gcg   4647
Glu Leu Lys Arg Lys Gln Asp Asp Ala Asp Gln Asp Met Met Met Ala
1470               1475                1480                1485

ggg atg gct tcg caa gcc gct cag gag gct gag ctc aat gcc aga aag   4695
Gly Met Ala Ser Gln Ala Ala Gln Glu Ala Glu Leu Asn Ala Arg Lys
               1490                1495                1500

gcc aaa aac tct gtc agc agc ctc ctc agc cag ctg aac aac ctc ttg   4743
Ala Lys Asn Ser Val Ser Ser Leu Leu Ser Gln Leu Asn Asn Leu Leu
          1505                1510                1515

gat cag cta gga cag ctg gac aca gtg gac ctg aac aag ctc aat gag   4791
Asp Gln Leu Gly Gln Leu Asp Thr Val Asp Leu Asn Lys Leu Asn Glu
       1520                1525                1530

atc gaa ggc tcc ctg aac aaa gcc aaa gac gaa atg aag gcc agc gac   4839
Ile Glu Gly Ser Leu Asn Lys Ala Lys Asp Glu Met Lys Ala Ser Asp
   1535                1540                1545

ctg gac agg aag gtg tct gac ctg gag agc gag gct cgg aag cag gaa   4887
Leu Asp Arg Lys Val Ser Asp Leu Glu Ser Glu Ala Arg Lys Gln Glu
1550               1555                1560                1565

gca gcc atc atg gac tat aac cgg gac ata gca gag atc att aag gat   4935
Ala Ala Ile Met Asp Tyr Asn Arg Asp Ile Ala Glu Ile Ile Lys Asp
               1570                1575                1580

att cac aac ctg gag gac atc aag aag acc cta cca acc ggc tgc ttc   4983
Ile His Asn Leu Glu Asp Ile Lys Lys Thr Leu Pro Thr Gly Cys Phe
          1585                1590                1595

aac acc ccg tct atc gag aag ccc tag tggcgagagg gctgtaaggc         5030
Asn Thr Pro Ser Ile Glu Lys Pro
       1600                1605

agtgtccctg acaggggacc ctgtgaggcc tcggtgcctt gacacaaaga ttacactttt 5090
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cagaccccca cttctctgct gctctccatc actgtccttt tgacccaaga aaagtcagag 5150

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ctctcctcca cttctgtcag caccctaccg gaactttccc ttgtttgcct gaagtcacgg 5270

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gccttaatct ctacagcctt ccccccctcag ggagggcaat aaagcgcaac acttggcatt 7490

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Leu Trp Pro Leu Leu Ala Val Leu Ala Ala Val Ala Gly Cys Val Arg
             20                  25                  30

Ala Ala Met Asp Glu Cys Ala Asp Glu Gly Gly Arg Pro Gln Arg Cys
         35                  40                  45

Met Pro Glu Phe Val Asn Ala Ala Phe Asn Val Thr Val Val Ala Thr
     50                  55                  60

Asn Thr Cys Gly Thr Pro Pro Glu Glu Tyr Cys Val Gln Thr Gly Val
 65                  70                  75                  80

Thr Gly Val Thr Lys Ser Cys His Leu Cys Asp Ala Gly Gln Gln His
                 85                  90                  95

Leu Gln His Gly Ala Ala Phe Leu Thr Asp Tyr Asn Asn Gln Ala Asp
            100                 105                 110

Thr Thr Trp Trp Gln Ser Gln Thr Met Leu Ala Gly Val Gln Tyr Pro
        115                 120                 125

Asn Ser Ile Asn Leu Thr Leu His Leu Gly Lys Ala Phe Asp Ile Thr
    130                 135                 140

Tyr Val Arg Leu Lys Phe His Thr Ser Arg Pro Glu Ser Phe Ala Ile
145                 150                 155                 160

Tyr Lys Arg Thr Arg Glu Asp Gly Pro Trp Ile Pro Tyr Gln Tyr Tyr
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165 170 175

Ser Gly Ser Cys Glu Asn Thr Tyr Ser Lys Ala Asn Arg Gly Phe Ile
180 185 190

Arg Thr Gly Gly Asp Glu Gln Gln Ala Leu Cys Thr Asp Glu Phe Ser
195 200 205

Asp Ile Ser Pro Leu Thr Gly Gly Asn Val Ala Phe Ser Thr Leu Glu
210 215 220

Gly Arg Pro Ser Ala Tyr Asn Phe Asp Asn Ser Pro Val Leu Gln Glu
225 230 235 240

Trp Val Thr Ala Thr Asp Ile Arg Val Thr Leu Asn Arg Leu Asn Thr
245 250 255

Phe Gly Asp Glu Val Phe Asn Asp Pro Lys Val Leu Lys Ser Tyr Tyr
260 265 270

Tyr Ala Ile Ser Asp Phe Ala Val Gly Gly Arg Cys Lys Cys Asn Gly
275 280 285

His Ala Ser Glu Cys Val Lys Asn Glu Phe Asp Lys Leu Met Cys Asn
290 295 300

Cys Lys His Asn Thr Tyr Gly Val Asp Cys Glu Lys Cys Leu Pro Phe
305 310 315 320

Phe Asn Asp Arg Pro Trp Arg Arg Ala Thr Ala Glu Ser Ala Ser Glu
325 330 335

Cys Leu Pro Cys Asp Cys Asn Gly Arg Ser Gln Glu Cys Tyr Phe Asp
340 345 350

Pro Glu Leu Tyr Arg Ser Thr Gly His Gly Gly His Cys Thr Asn Cys
355 360 365

Arg Asp Asn Thr Asp Gly Ala Lys Cys Glu Arg Cys Arg Glu Asn Phe
370 375 380

Phe Arg Leu Gly Asn Thr Glu Ala Cys Ser Pro Cys His Cys Ser Pro
385 390 395 400

Val Gly Ser Leu Ser Thr Gln Cys Asp Ser Tyr Gly Arg Cys Ser Cys
405 410 415

Lys Pro Gly Val Met Gly Asp Lys Cys Asp Arg Cys Gln Pro Gly Phe
420 425 430

His Ser Leu Thr Glu Ala Gly Cys Arg Pro Cys Ser Cys Asp Pro Ser
435 440 445

Gly Ser Thr Asp Glu Cys Asn Val Glu Thr Gly Arg Cys Val Cys Lys
450 455 460

Asp Asn Val Glu Gly Phe Asn Cys Glu Arg Cys Lys Pro Gly Phe Phe
465 470 475 480

Asn Leu Glu Ser Ser Asn Pro Lys Gly Cys Thr Pro Cys Phe Cys Phe
485 490 495

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Gly His Ser Ser Val Cys Thr Asn Ala Val Gly Tyr Ser Val Tyr Asp
           500                 505                 510

Ile Ser Ser Thr Phe Gln Ile Asp Glu Asp Gly Trp Arg Val Glu Gln
       515                 520                 525

Arg Asp Gly Ser Glu Ala Ser Leu Glu Trp Ser Ser Asp Arg Gln Tyr
   530                 535                 540

Ile Ala Val Ile Ser Asp Ser Tyr Phe Pro Arg Tyr Phe Ile Ala Pro
545                 550                 555                 560

Val Lys Phe Leu Gly Asn Gln Val Leu Ser Tyr Gly Gln Asn Leu Ser
               565                 570                 575

Phe Ser Phe Arg Val Asp Arg Arg Asp Thr Arg Leu Ser Ala Glu Asp
           580                 585                 590

Leu Val Leu Glu Gly Ala Gly Leu Arg Val Ser Val Pro Leu Ile Ala
       595                 600                 605

Gln Gly Asn Ser Tyr Pro Ser Glu Thr Thr Val Lys Tyr Ile Phe Arg
   610                 615                 620

Leu His Glu Ala Thr Asp Tyr Pro Trp Arg Pro Ala Leu Ser Pro Phe
625                 630                 635                 640

Glu Phe Gln Lys Leu Leu Asn Asn Leu Thr Ser Ile Lys Ile Arg Gly
               645                 650                 655

Thr Tyr Ser Glu Arg Ser Ala Gly Tyr Leu Asp Asp Val Thr Leu Gln
           660                 665                 670

Ser Ala Arg Pro Gly Pro Gly Val Pro Ala Thr Trp Val Glu Ser Cys
       675                 680                 685

Thr Cys Pro Val Gly Tyr Gly Gly Gln Phe Cys Glu Thr Cys Leu Pro
   690                 695                 700

Gly Tyr Arg Arg Glu Thr Pro Ser Leu Gly Pro Tyr Ser Pro Cys Val
705                 710                 715                 720

Leu Cys Thr Cys Asn Gly His Ser Glu Thr Cys Asp Pro Glu Thr Gly
               725                 730                 735

Val Cys Asp Cys Arg Asp Asn Thr Ala Gly Pro His Cys Glu Lys Cys
           740                 745                 750

Ser Asp Gly Tyr Tyr Gly Asp Ser Thr Leu Gly Thr Ser Ser Asp Cys
       755                 760                 765

Gln Pro Cys Pro Cys Pro Gly Gly Ser Ser Cys Ala Ile Val Pro Lys
   770                 775                 780

Thr Lys Glu Val Val Cys Thr His Cys Pro Thr Gly Thr Ala Gly Lys
785                 790                 795                 800

Arg Cys Glu Leu Cys Asp Asp Gly Tyr Phe Gly Asp Pro Leu Gly Ser
               805                 810                 815
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Asn Gly Pro Val Arg Leu Cys Arg Pro Cys Gln Cys Asn Asp Asn Ile
820 825 830

Asp Pro Asn Ala Val Gly Asn Cys Asn Arg Leu Thr Gly Glu Cys Leu
835 840 845

Lys Cys Ile Tyr Asn Thr Ala Gly Phe Tyr Cys Asp Arg Cys Lys Glu
850 855 860

Gly Phe Phe Gly Asn Pro Leu Ala Pro Asn Pro Ala Asp Lys Cys Lys
865 870 875 880

Ala Cys Ala Cys Asn Tyr Gly Thr Val Gln Gln Gln Ser Ser Cys Asn
885 890 895

Pro Val Thr Gly Gln Cys Gln Cys Leu Pro His Val Ser Gly Arg Asp
900 905 910

Cys Gly Thr Cys Asp Pro Gly Tyr Tyr Asn Leu Gln Ser Gly Gln Gly
915 920 925

Cys Glu Arg Cys Asp Cys His Ala Leu Gly Ser Thr Asn Gly Gln Cys
930 935 940

Asp Ile Arg Thr Gly Gln Cys Glu Cys Gln Pro Gly Ile Thr Gly Gln
945 950 955 960

His Cys Glu Arg Cys Glu Thr Asn His Phe Gly Phe Gly Pro Glu Gly
965 970 975

Cys Lys Pro Cys Asp Cys His His Glu Gly Ser Leu Ser Leu Gln Cys
980 985 990

Lys Asp Asp Gly Arg Cys Glu Cys Arg Glu Gly Phe Val Gly Asn Arg
995 1000 1005

Cys Asp Gln Cys Glu Glu Asn Tyr Phe Tyr Asn Arg Ser Trp Pro Gly
1010 1015 1020

Cys Gln Glu Cys Pro Ala Cys Tyr Arg Leu Val Lys Asp Lys Ala Ala
025 1030 1035 1040

Glu His Arg Val Lys Leu Gln Glu Leu Glu Ser Leu Ile Ala Asn Leu
1045 1050 1055

Gly Thr Gly Asp Asp Met Val Thr Asp Gln Ala Phe Glu Asp Arg Leu
1060 1065 1070

Lys Glu Ala Glu Arg Glu Val Thr Asp Leu Leu Arg Glu Ala Gln Glu
1075 1080 1085

Val Lys Asp Val Asp Gln Asn Leu Met Asp Arg Leu Gln Arg Val Asn
1090 1095 1100

Ser Ser Leu His Ser Gln Ile Ser Arg Leu Gln Asn Ile Arg Asn Thr
105 1110 1115 1120

Ile Glu Glu Thr Gly Ile Leu Ala Glu Arg Ala Arg Ser Arg Val Glu
1125 1130 1135

Ser Thr Glu Gln Leu Ile Glu Ile Ala Ser Arg Glu Leu Glu Lys Ala

1140 1145 1150

Lys Met Ala Ala Asn Val Ser Ile Thr Gln Pro Glu Ser Thr Gly Glu
1155 1160 1165

Pro Asn Asn Met Thr Leu Leu Ala Glu Glu Ala Arg Arg Leu Ala Glu
1170 1175 1180

Arg His Lys Gln Glu Ala Asp Asp Ile Val Arg Val Ala Lys Thr Ala
185 1190 1195 1200

Asn Glu Thr Ser Ala Glu Ala Tyr Asn Leu Leu Leu Arg Thr Leu Ala
1205 1210 1215

Gly Glu Asn Gln Thr Ala Leu Glu Ile Glu Glu Leu Asn Arg Lys Tyr
1220 1225 1230

Glu Gln Ala Lys Asn Ile Ser Gln Asp Leu Glu Lys Gln Ala Ala Arg
1235 1240 1245

Val His Glu Glu Ala Lys Arg Ala Gly Asp Lys Ala Val Glu Ile Tyr
1250 1255 1260

Ala Ser Val Ala Gln Leu Thr Pro Val Asp Ser Glu Ala Leu Glu Asn
265 1270 1275 1280

Glu Ala Asn Lys Ile Lys Lys Glu Ala Ala Asp Leu Asp Arg Leu Ile
1285 1290 1295

Asp Gln Lys Leu Lys Asp Tyr Glu Asp Leu Arg Glu Asp Met Arg Gly
1300 1305 1310

Lys Glu His Glu Val Lys Asn Leu Leu Glu Lys Gly Lys Ala Glu Gln
1315 1320 1325

Gln Thr Ala Asp Gln Leu Leu Ala Arg Ala Asp Ala Ala Lys Ala Leu
1330 1335 1340

Ala Glu Glu Ala Ala Lys Lys Gly Arg Ser Thr Leu Gln Glu Ala Asn
345 1350 1355 1360

Asp Ile Leu Asn Asn Leu Lys Asp Phe Asp Arg Arg Val Asn Asp Asn
1365 1370 1375

Lys Thr Ala Ala Glu Glu Ala Leu Arg Arg Ile Pro Ala Ile Asn Arg
1380 1385 1390

Thr Ile Ala Glu Ala Asn Glu Lys Thr Arg Glu Ala Gln Leu Ala Leu
1395 1400 1405

Gly Asn Ala Ala Ala Asp Ala Thr Glu Ala Lys Asn Lys Ala His Glu
1410 1415 1420

Ala Glu Arg Ile Ala Ser Ala Ala Gln Lys Asn Ala Thr Ser Thr Lys
425 1430 1435 1440

Ala Asp Ala Glu Arg Thr Phe Gly Glu Val Thr Asp Leu Asp Asn Glu
1445 1450 1455

Val Asn Gly Met Leu Arg Gln Leu Glu Glu Ala Glu Asn Glu Leu Lys
1460 1465 1470

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Arg Lys Gln Asp Asp Ala Asp Gln Asp Met Met Met Ala Gly Met Ala
       1475                1480                1485

Ser Gln Ala Ala Gln Glu Ala Glu Leu Asn Ala Arg Lys Ala Lys Asn
   1490                1495                1500

Ser Val Ser Ser Leu Leu Ser Gln Leu Asn Asn Leu Leu Asp Gln Leu
505                1510                1515                1520

Gly Gln Leu Asp Thr Val Asp Leu Asn Lys Leu Asn Glu Ile Glu Gly
               1525                1530                1535

Ser Leu Asn Lys Ala Lys Asp Glu Met Lys Ala Ser Asp Leu Asp Arg
          1540                1545                1550

Lys Val Ser Asp Leu Glu Ser Glu Ala Arg Lys Gln Glu Ala Ala Ile
       1555                1560                1565

Met Asp Tyr Asn Arg Asp Ile Ala Glu Ile Ile Lys Asp Ile His Asn
   1570                1575                1580

Leu Glu Asp Ile Lys Lys Thr Leu Pro Thr Gly Cys Phe Asn Thr Pro
585                1590                1595                1600

Ser Ile Glu Lys Pro
               1605


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Ala Met Asp Glu Cys Ala Asp Glu Gly Gly Arg Pro Gln Arg Cys Met
  1               5                  10                  15

ccg gag ttt gtt aat gcc gcc ttc aat gtg acc gtg gtg gct acc aac   96
Pro Glu Phe Val Asn Ala Ala Phe Asn Val Thr Val Val Ala Thr Asn
            20                  25                  30

acg tgt ggg act ccg ccc gag gag tac tgc gtg cag act ggg gtg acc   144
Thr Cys Gly Thr Pro Pro Glu Glu Tyr Cys Val Gln Thr Gly Val Thr
        35                  40                  45

gga gtc act aag tcc tgt cac ctg tgc gac gcc ggc cag cag cac ctg   192
Gly Val Thr Lys Ser Cys His Leu Cys Asp Ala Gly Gln Gln His Leu
    50                  55                  60

caa cac ggg gca gcc ttc ctg acc gac tac aac aac cag gcc gac acc   240
Gln His Gly Ala Ala Phe Leu Thr Asp Tyr Asn Asn Gln Ala Asp Thr
65                  70                  75                  80

acc tgg tgg caa agc cag act atg ctg gcc ggg gtg cag tac ccc aac   288
Thr Trp Trp Gln Ser Gln Thr Met Leu Ala Gly Val Gln Tyr Pro Asn
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                    85                  90                  95

tcc atc aac ctc acg ctg cac ctg gga aag gct ttt gac atc act tac   336
Ser Ile Asn Leu Thr Leu His Leu Gly Lys Ala Phe Asp Ile Thr Tyr
            100                 105                 110

gtg cgc ctc aag ttc cac acc agc cgt cca gag agc ttc gcc atc tat   384
Val Arg Leu Lys Phe His Thr Ser Arg Pro Glu Ser Phe Ala Ile Tyr
        115                 120                 125

aag cgc act cgg gaa gac ggg ccc tgg att cct tat cag tac tac agt   432
Lys Arg Thr Arg Glu Asp Gly Pro Trp Ile Pro Tyr Gln Tyr Tyr Ser
    130                 135                 140

ggg tcc tgt gag aac acg tac tca aag gct aac cgt ggc ttc atc agg   480
Gly Ser Cys Glu Asn Thr Tyr Ser Lys Ala Asn Arg Gly Phe Ile Arg
145                 150                 155                 160

acc gga ggg gac gag cag cag gcc ttg tgt act gat gaa ttc agt gac   528
Thr Gly Gly Asp Glu Gln Gln Ala Leu Cys Thr Asp Glu Phe Ser Asp
                165                 170                 175

att tcc ccc ctc acc ggt ggc aac gtg gcc ttt tca acc ctg gaa gga   576
Ile Ser Pro Leu Thr Gly Gly Asn Val Ala Phe Ser Thr Leu Glu Gly
            180                 185                 190

cgg ccg agt gcc tac aac ttt gac aac agc cct gtg ctc cag gaa tgg   624
Arg Pro Ser Ala Tyr Asn Phe Asp Asn Ser Pro Val Leu Gln Glu Trp
        195                 200                 205

gta act gcc act gac atc aga gtg acg ctc aat cgc ctg aac acc ttt   672
Val Thr Ala Thr Asp Ile Arg Val Thr Leu Asn Arg Leu Asn Thr Phe
    210                 215                 220

gga gat gaa gtg ttt aac gac ccc aaa gtt ctc aag tct tac tat tac   720
Gly Asp Glu Val Phe Asn Asp Pro Lys Val Leu Lys Ser Tyr Tyr Tyr
225                 230                 235                 240

gca atc tca gac ttt gct gtg ggc ggc agg tgt aaa tgt aac gga cat   768
Ala Ile Ser Asp Phe Ala Val Gly Gly Arg Cys Lys Cys Asn Gly His
                245                 250                 255

gcc agc gag tgt gta aag aac gag ttt gac aaa ctc atg tgc aac tgc   816
Ala Ser Glu Cys Val Lys Asn Glu Phe Asp Lys Leu Met Cys Asn Cys
            260                 265                 270

aaa cat aac aca tac gga gtt gac tgt gaa aag tgc ctg cct ttc ttc   864
Lys His Asn Thr Tyr Gly Val Asp Cys Glu Lys Cys Leu Pro Phe Phe
        275                 280                 285

aat gac cgg ccg tgg agg agg gcg act gct gag agc gcc agc gag tgc   912
Asn Asp Arg Pro Trp Arg Arg Ala Thr Ala Glu Ser Ala Ser Glu Cys
    290                 295                 300

ctt cct tgt gac tgc aat ggc cga tcc caa gag tgc tac ttt gat cct   960
Leu Pro Cys Asp Cys Asn Gly Arg Ser Gln Glu Cys Tyr Phe Asp Pro
305                 310                 315                 320

gaa cta tac cgt tcc act gga cat ggt ggc cac tgt acc aac tgc cgg   1008
Glu Leu Tyr Arg Ser Thr Gly His Gly Gly His Cys Thr Asn Cys Arg
                325                 330                 335
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gat aac aca gat ggt gcc aag tgc gag agg tgc cgg gag aat ttc ttc   1056
Asp Asn Thr Asp Gly Ala Lys Cys Glu Arg Cys Arg Glu Asn Phe Phe
            340                 345                 350

cgc ctg ggg aac act gaa gcc tgc tct ccg tgc cac tgc agc cct gtt   1104
Arg Leu Gly Asn Thr Glu Ala Cys Ser Pro Cys His Cys Ser Pro Val
        355                 360                 365

ggt tct ctc agc aca cag tgt gac agt tac ggc aga tgc agc tgt aag   1152
Gly Ser Leu Ser Thr Gln Cys Asp Ser Tyr Gly Arg Cys Ser Cys Lys
    370                 375                 380

cca gga gtg atg ggt gac aag tgt gac cgt tgt cag cct ggg ttc cat   1200
Pro Gly Val Met Gly Asp Lys Cys Asp Arg Cys Gln Pro Gly Phe His
385                 390                 395                 400

tcc ctc act gag gca gga tgc agg cca tgc tcc tgc gat cct tcg ggc   1248
Ser Leu Thr Glu Ala Gly Cys Arg Pro Cys Ser Cys Asp Pro Ser Gly
                405                 410                 415

agc aca gac gag tgt aat gtt gaa aca gga aga tgc gtt tgc aaa gac   1296
Ser Thr Asp Glu Cys Asn Val Glu Thr Gly Arg Cys Val Cys Lys Asp
            420                 425                 430

aat gtt gaa ggc ttc aac tgt gag aga tgc aaa cct gga ttt ttt aat   1344
Asn Val Glu Gly Phe Asn Cys Glu Arg Cys Lys Pro Gly Phe Phe Asn
        435                 440                 445

ctg gag tca tct aat cct aag ggc tgc aca ccc tgc ttc tgc ttt ggc   1392
Leu Glu Ser Ser Asn Pro Lys Gly Cys Thr Pro Cys Phe Cys Phe Gly
    450                 455                 460

cat tct tct gtg tgc aca aat gct gtt ggc tac agt gtt tat gac atc   1440
His Ser Ser Val Cys Thr Asn Ala Val Gly Tyr Ser Val Tyr Asp Ile
465                 470                 475                 480

tcc tcc acc ttt cag att gat gag gat ggg tgg cgc gtg gag cag aga   1488
Ser Ser Thr Phe Gln Ile Asp Glu Asp Gly Trp Arg Val Glu Gln Arg
                485                 490                 495

gat ggc tcg gag gcg tct ctg gag tgg tcc tca gac agg caa tat att   1536
Asp Gly Ser Glu Ala Ser Leu Glu Trp Ser Ser Asp Arg Gln Tyr Ile
            500                 505                 510

gcc gta atc tca gac agt tac ttt cct aga tac ttc atc gcc cct gtg   1584
Ala Val Ile Ser Asp Ser Tyr Phe Pro Arg Tyr Phe Ile Ala Pro Val
        515                 520                 525

aag ttc ctg ggc aac cag gtc ctg agt tat ggg cag aat ctt tcc ttc   1632
Lys Phe Leu Gly Asn Gln Val Leu Ser Tyr Gly Gln Asn Leu Ser Phe
    530                 535                 540

tcc ttc cga gtg gac aga cga gac act cgc ctc tcc gca gag gac ctt   1680
Ser Phe Arg Val Asp Arg Arg Asp Thr Arg Leu Ser Ala Glu Asp Leu
545                 550                 555                 560

gtg ctc gaa gga gct ggc ttg aga gta tcc gtg ccc ttg atc gct cag   1728
Val Leu Glu Gly Ala Gly Leu Arg Val Ser Val Pro Leu Ile Ala Gln
                565                 570                 575
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ggc aac tcc tac ccc agc gag acc act gtg aag tac atc ttc agg ctc   1776
Gly Asn Ser Tyr Pro Ser Glu Thr Thr Val Lys Tyr Ile Phe Arg Leu
            580                 585                 590

cat gaa gca acg gat tac cct tgg agg ccc gct ctc tcc ccg ttt gaa   1824
His Glu Ala Thr Asp Tyr Pro Trp Arg Pro Ala Leu Ser Pro Phe Glu
        595                 600                 605

ttt cag aag ctc ctg aac aac ttg acc tct atc aag atc cgt ggt aca   1872
Phe Gln Lys Leu Leu Asn Asn Leu Thr Ser Ile Lys Ile Arg Gly Thr
    610                 615                 620

tac agc gag agg agc gct ggg tac ttg gat gat gtc acc ttg caa agt   1920
Tyr Ser Glu Arg Ser Ala Gly Tyr Leu Asp Asp Val Thr Leu Gln Ser
625                 630                 635                 640

gct cgc cct ggg ccc gga gtc cct gca acg tgg gtg gag tcc tgc acc   1968
Ala Arg Pro Gly Pro Gly Val Pro Ala Thr Trp Val Glu Ser Cys Thr
                645                 650                 655

tgt cca gtg gga tac ggg gga cag ttc tgt gag acg tgc ctc cca ggg   2016
Cys Pro Val Gly Tyr Gly Gly Gln Phe Cys Glu Thr Cys Leu Pro Gly
            660                 665                 670

tac aga aga gaa act cca agc ctt gga cct tat agc ccg tgt gtg ctc   2064
Tyr Arg Arg Glu Thr Pro Ser Leu Gly Pro Tyr Ser Pro Cys Val Leu
        675                 680                 685

tgt acc tgt aat ggg cac agt gag acc tgt gac ccg gag aca ggt gtc   2112
Cys Thr Cys Asn Gly His Ser Glu Thr Cys Asp Pro Glu Thr Gly Val
    690                 695                 700

tgt gac tgc aga gac aat aca gcc ggc ccc cac tgt gag aaa tgt agc   2160
Cys Asp Cys Arg Asp Asn Thr Ala Gly Pro His Cys Glu Lys Cys Ser
705                 710                 715                 720

gat ggg tac tat ggg gac tca acc ctg ggc acc tcc tct gac tgc cag   2208
Asp Gly Tyr Tyr Gly Asp Ser Thr Leu Gly Thr Ser Ser Asp Cys Gln
                725                 730                 735

cct tgt ccc tgc ccc ggt ggc tca agt tgt gcc att gtc cca aag aca   2256
Pro Cys Pro Cys Pro Gly Gly Ser Ser Cys Ala Ile Val Pro Lys Thr
            740                 745                 750

aag gaa gtg gtg tgc acg cac tgt ccg act ggc act gcc ggc aag aga   2304
Lys Glu Val Val Cys Thr His Cys Pro Thr Gly Thr Ala Gly Lys Arg
        755                 760                 765

tgt gaa ctc tgt gat gac ggc tac ttt gga gac cct ctg ggc agc aat   2352
Cys Glu Leu Cys Asp Asp Gly Tyr Phe Gly Asp Pro Leu Gly Ser Asn
    770                 775                 780

ggg ccc gtg aga ctg tgc cgc ccg tgc cag tgt aac gac aac ata gac   2400
Gly Pro Val Arg Leu Cys Arg Pro Cys Gln Cys Asn Asp Asn Ile Asp
785                 790                 795                 800

ccc aac gcg gtt ggc aac tgc aac cgc ctg acg ggc gag tgc ctg aag   2448
Pro Asn Ala Val Gly Asn Cys Asn Arg Leu Thr Gly Glu Cys Leu Lys
                805                 810                 815

tgc atc tat aac acg gct ggt ttc tac tgc gac cgg tgc aag gaa ggg   2496
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Cys Ile Tyr Asn Thr Ala Gly Phe Tyr Cys Asp Arg Cys Lys Glu Gly
            820                 825                 830

ttt ttc gga aat ccc ctg gct ccc aat cca gcc gac aaa tgc aaa gcc   2544
Phe Phe Gly Asn Pro Leu Ala Pro Asn Pro Ala Asp Lys Cys Lys Ala
        835                 840                 845

tgc gcc tgc aac tac ggg aca gtg cag caa cag agc agc tgt aac ccg   2592
Cys Ala Cys Asn Tyr Gly Thr Val Gln Gln Gln Ser Ser Cys Asn Pro
    850                 855                 860

gtg acc gga caa tgc cag tgt ctg cct cat gtg tct ggc cgc gac tgc   2640
Val Thr Gly Gln Cys Gln Cys Leu Pro His Val Ser Gly Arg Asp Cys
865                 870                 875                 880

ggt act tgt gac cct ggc tac tac aac ctg cag agc ggg caa ggc tgc   2688
Gly Thr Cys Asp Pro Gly Tyr Tyr Asn Leu Gln Ser Gly Gln Gly Cys
                885                 890                 895

gag agg tgt gac tgc cat gct ttg ggt tcc acc aat ggg cag tgt gac   2736
Glu Arg Cys Asp Cys His Ala Leu Gly Ser Thr Asn Gly Gln Cys Asp
            900                 905                 910

atc cgc acc ggg cag tgt gag tgc cag cct ggc atc acc ggt cag cac   2784
Ile Arg Thr Gly Gln Cys Glu Cys Gln Pro Gly Ile Thr Gly Gln His
        915                 920                 925

tgt gag cgc tgt gag acc aac cac ttt ggg ttt gga cct gaa ggc tgc   2832
Cys Glu Arg Cys Glu Thr Asn His Phe Gly Phe Gly Pro Glu Gly Cys
    930                 935                 940

aaa cct tgt gac tgt cac cat gaa gga tcc ctt tcg ctc cag tgt aaa   2880
Lys Pro Cys Asp Cys His His Glu Gly Ser Leu Ser Leu Gln Cys Lys
945                 950                 955                 960

gac gac ggc cgt tgt gaa tgc agg gaa ggc ttt gtg ggc aat cgc tgt   2928
Asp Asp Gly Arg Cys Glu Cys Arg Glu Gly Phe Val Gly Asn Arg Cys
                965                 970                 975

gac cag tgt gaa gag aac tat ttc tac aat cgg tcc tgg cct ggc tgc   2976
Asp Gln Cys Glu Glu Asn Tyr Phe Tyr Asn Arg Ser Trp Pro Gly Cys
            980                 985                 990

cag gag tgt ccg gct tgt tac cga ctt gtg aag gat aag gct gct gag   3024
Gln Glu Cys Pro Ala Cys Tyr Arg Leu Val Lys Asp Lys Ala Ala Glu
        995                1000                1005

cat cga gtg aaa ctc cag gag tta gag agc ctc atc gcc aac ctt ggc   3072
His Arg Val Lys Leu Gln Glu Leu Glu Ser Leu Ile Ala Asn Leu Gly
   1010                1015                1020

act ggg gat gac atg gtg aca gat caa gcc ttt gag gac aga ctt aag   3120
Thr Gly Asp Asp Met Val Thr Asp Gln Ala Phe Glu Asp Arg Leu Lys
1025                1030                1035                1040

gaa gca gaa agg gag gtg aca gac ctt ctc cgt gag gct cag gaa gtc   3168
Glu Ala Glu Arg Glu Val Thr Asp Leu Leu Arg Glu Ala Gln Glu Val
               1045                1050                1055

aaa gat gta gat caa aat ctg atg gat cgc ctt cag aga gta aat agc   3216
Lys Asp Val Asp Gln Asn Leu Met Asp Arg Leu Gln Arg Val Asn Ser
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          1060                1065                1070

agc ctg cat agc caa att agc cga ctg cag aat atc cgg aat act atc   3264
Ser Leu His Ser Gln Ile Ser Arg Leu Gln Asn Ile Arg Asn Thr Ile
       1075                1080                1085

gaa gag acc ggg atc ttg gct gag cga gca cgg tcc cga gtg gag agt   3312
Glu Glu Thr Gly Ile Leu Ala Glu Arg Ala Arg Ser Arg Val Glu Ser
   1090                1095                1100

aca gag cag ctg att gag atc gcc tcc agg gag ctc gag aaa gca aaa   3360
Thr Glu Gln Leu Ile Glu Ile Ala Ser Arg Glu Leu Glu Lys Ala Lys
1105                1110                1115                1120

atg gcc gcc aat gtg tca atc act cag cca gag tct aca ggg gag cca   3408
Met Ala Ala Asn Val Ser Ile Thr Gln Pro Glu Ser Thr Gly Glu Pro
               1125                1130                1135

aac aac atg acc ctc ttg gca gaa gaa gcc cga agg ctt gca gag cgt   3456
Asn Asn Met Thr Leu Leu Ala Glu Glu Ala Arg Arg Leu Ala Glu Arg
          1140                1145                1150

cat aaa cag gaa gcc gat gac att gta cga gtg gca aag aca gcc aac   3504
His Lys Gln Glu Ala Asp Asp Ile Val Arg Val Ala Lys Thr Ala Asn
       1155                1160                1165

gag act tca gct gag gca tat aat ctg ctt ttg agg acc ctg gca gga   3552
Glu Thr Ser Ala Glu Ala Tyr Asn Leu Leu Leu Arg Thr Leu Ala Gly
   1170                1175                1180

gaa aat caa act gcg ctg gag att gaa gaa ctt aac cgg aag tac gaa   3600
Glu Asn Gln Thr Ala Leu Glu Ile Glu Glu Leu Asn Arg Lys Tyr Glu
1185                1190                1195                1200

caa gca aag aac atc tct cag gac ctg gag aag cag gct gcc cga gtc   3648
Gln Ala Lys Asn Ile Ser Gln Asp Leu Glu Lys Gln Ala Ala Arg Val
               1205                1210                1215

cat gag gaa gcc aag cgt gca ggt gac aaa gcc gta gag atc tat gcc   3696
His Glu Glu Ala Lys Arg Ala Gly Asp Lys Ala Val Glu Ile Tyr Ala
          1220                1225                1230

agt gtg gcc cag ctg acc cct gtg gac tct gag gcc ctg gag aat gaa   3744
Ser Val Ala Gln Leu Thr Pro Val Asp Ser Glu Ala Leu Glu Asn Glu
       1235                1240                1245

gca aat aaa atc aag aaa gaa gct gca gac ctg gac cgt ctg att gac   3792
Ala Asn Lys Ile Lys Lys Glu Ala Ala Asp Leu Asp Arg Leu Ile Asp
   1250                1255                1260

cag aag cta aag gat tac gag gac ctc agg gaa gac atg aga gga aag   3840
Gln Lys Leu Lys Asp Tyr Glu Asp Leu Arg Glu Asp Met Arg Gly Lys
1265                1270                1275                1280

gaa cat gaa gtg aag aac ctt cta gag aag ggg aaa gct gaa cag cag   3888
Glu His Glu Val Lys Asn Leu Leu Glu Lys Gly Lys Ala Glu Gln Gln
               1285                1290                1295

acc gcc gac caa ctc cta gct cga gcc gat gct gcc aag gcc ctt gct   3936
Thr Ala Asp Gln Leu Leu Ala Arg Ala Asp Ala Ala Lys Ala Leu Ala
          1300                1305                1310
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gaa gaa gct gct aag aag gga cgc agt acc tta caa gaa gcc aat gac   3984
Glu Glu Ala Ala Lys Lys Gly Arg Ser Thr Leu Gln Glu Ala Asn Asp
       1315                1320                1325

att ctc aac aac ctg aaa gat ttt gat aga cgt gtg aac gat aac aag   4032
Ile Leu Asn Asn Leu Lys Asp Phe Asp Arg Arg Val Asn Asp Asn Lys
   1330                1335                1340

aca gcc gcg gaa gaa gct cta agg aga att ccc gcc atc aac cgg acc   4080
Thr Ala Ala Glu Glu Ala Leu Arg Arg Ile Pro Ala Ile Asn Arg Thr
1345                1350                1355                1360

ata gct gaa gcc aat gag aag aca agg gag gcc cag cta gcg ctg ggc   4128
Ile Ala Glu Ala Asn Glu Lys Thr Arg Glu Ala Gln Leu Ala Leu Gly
               1365                1370                1375

aat gct gcc gct gac gcc acg gag gcc aag aac aag gcc cat gag gca   4176
Asn Ala Ala Ala Asp Ala Thr Glu Ala Lys Asn Lys Ala His Glu Ala
          1380                1385                1390

gag agg atc gcc agc gcc gcg cag aag aat gcc acc agt acc aag gcg   4224
Glu Arg Ile Ala Ser Ala Ala Gln Lys Asn Ala Thr Ser Thr Lys Ala
       1395                1400                1405

gac gca gaa aga acc ttc ggg gaa gtt aca gat ctg gat aat gag gtg   4272
Asp Ala Glu Arg Thr Phe Gly Glu Val Thr Asp Leu Asp Asn Glu Val
   1410                1415                1420

aac ggt atg ctg agg cag cta gag gag gca gag aat gag ctg aag agg   4320
Asn Gly Met Leu Arg Gln Leu Glu Glu Ala Glu Asn Glu Leu Lys Arg
1425                1430                1435                1440

aag caa gat gac gcc gac cag gac atg atg atg gcg ggg atg gct tcg   4368
Lys Gln Asp Asp Ala Asp Gln Asp Met Met Met Ala Gly Met Ala Ser
               1445                1450                1455

caa gcc gct cag gag gct gag ctc aat gcc aga aag gcc aaa aac tct   4416
Gln Ala Ala Gln Glu Ala Glu Leu Asn Ala Arg Lys Ala Lys Asn Ser
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gtc agc agc ctc ctc agc cag ctg aac aac ctc ttg gat cag cta gga   4464
Val Ser Ser Leu Leu Ser Gln Leu Asn Asn Leu Leu Asp Gln Leu Gly
       1475                1480                1485

cag ctg gac aca gtg gac ctg aac aag ctc aat gag atc gaa ggc tcc   4512
Gln Leu Asp Thr Val Asp Leu Asn Lys Leu Asn Glu Ile Glu Gly Ser
   1490                1495                1500

ctg aac aaa gcc aaa gac gaa atg aag gcc agc gac ctg gac agg aag   4560
Leu Asn Lys Ala Lys Asp Glu Met Lys Ala Ser Asp Leu Asp Arg Lys
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gtg tct gac ctg gag agc gag gct cgg aag cag gaa gca gcc atc atg   4608
Val Ser Asp Leu Glu Ser Glu Ala Arg Lys Gln Glu Ala Ala Ile Met
               1525                1530                1535

gac tat aac cgg gac ata gca gag atc att aag gat att cac aac ctg   4656
Asp Tyr Asn Arg Asp Ile Ala Glu Ile Ile Lys Asp Ile His Asn Leu
          1540                1545                1550
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gag gac atc aag aag acc cta cca acc ggc tgc ttc aac acc ccg tct 4704
Glu Asp Ile Lys Lys Thr Leu Pro Thr Gly Cys Phe Asn Thr Pro Ser
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atc gag aag ccc tagtggcgag agggctgtaa ggcagtgtcc ctgacagggg 4756
Ile Glu Lys Pro
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Gly Val Thr Lys Ser Cys His Leu Cys Asp Ala Gly Gln Gln His Leu
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Gln His Gly Ala Ala Phe Leu Thr Asp Tyr Asn Asn Gln Ala Asp Thr
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Ser Ile Asn Leu Thr Leu His Leu Gly Lys Ala Phe Asp Ile Thr Tyr
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Val Arg Leu Lys Phe His Thr Ser Arg Pro Glu Ser Phe Ala Ile Tyr
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Lys Arg Thr Arg Glu Asp Gly Pro Trp Ile Pro Tyr Gln Tyr Tyr Ser
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Arg Leu Gly Asn Thr Glu Ala Cys Ser Pro Cys His Cys Ser Pro Val
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Gly Ser Leu Ser Thr Gln Cys Asp Ser Tyr Gly Arg Cys Ser Cys Lys
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Pro Gly Val Met Gly Asp Lys Cys Asp Arg Cys Gln Pro Gly Phe His
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Ser Thr Asp Glu Cys Asn Val Glu Thr Gly Arg Cys Val Cys Lys Asp
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Asn Val Glu Gly Phe Asn Cys Glu Arg Cys Lys Pro Gly Phe Phe Asn
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Leu Glu Ser Ser Asn Pro Lys Gly Cys Thr Pro Cys Phe Cys Phe Gly
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His Ser Ser Val Cys Thr Asn Ala Val Gly Tyr Ser Val Tyr Asp Ile
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Ser Ser Thr Phe Gln Ile Asp Glu Asp Gly Trp Arg Val Glu Gln Arg
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Asp Gly Ser Glu Ala Ser Leu Glu Trp Ser Ser Asp Arg Gln Tyr Ile
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Ala Val Ile Ser Asp Ser Tyr Phe Pro Arg Tyr Phe Ile Ala Pro Val
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Lys Phe Leu Gly Asn Gln Val Leu Ser Tyr Gly Gln Asn Leu Ser Phe
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Ser Phe Arg Val Asp Arg Arg Asp Thr Arg Leu Ser Ala Glu Asp Leu
545                 550                 555                 560

Val Leu Glu Gly Ala Gly Leu Arg Val Ser Val Pro Leu Ile Ala Gln
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Gly Asn Ser Tyr Pro Ser Glu Thr Thr Val Lys Tyr Ile Phe Arg Leu
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His Glu Ala Thr Asp Tyr Pro Trp Arg Pro Ala Leu Ser Pro Phe Glu
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Phe Gln Lys Leu Leu Asn Asn Leu Thr Ser Ile Lys Ile Arg Gly Thr
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625                 630                 635                 640

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Cys Pro Val Gly Tyr Gly Gly Gln Phe Cys Glu Thr Cys Leu Pro Gly
            660                 665                 670

Tyr Arg Arg Glu Thr Pro Ser Leu Gly Pro Tyr Ser Pro Cys Val Leu
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Cys Thr Cys Asn Gly His Ser Glu Thr Cys Asp Pro Glu Thr Gly Val
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Cys Asp Cys Arg Asp Asn Thr Ala Gly Pro His Cys Glu Lys Cys Ser
705                 710                 715                 720

Asp Gly Tyr Tyr Gly Asp Ser Thr Leu Gly Thr Ser Ser Asp Cys Gln
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Pro Cys Pro Cys Pro Gly Gly Ser Ser Cys Ala Ile Val Pro Lys Thr
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Lys Glu Val Val Cys Thr His Cys Pro Thr Gly Thr Ala Gly Lys Arg
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Cys Glu Leu Cys Asp Asp Gly Tyr Phe Gly Asp Pro Leu Gly Ser Asn
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Gln Glu Cys Pro Ala Cys Tyr Arg Leu Val Lys Asp Lys Ala Ala Glu
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Ser Leu His Ser Gln Ile Ser Arg Leu Gln Asn Ile Arg Asn Thr Ile
1075 1080 1085

Glu Glu Thr Gly Ile Leu Ala Glu Arg Ala Arg Ser Arg Val Glu Ser
1090 1095 1100

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Thr Glu Gln Leu Ile Glu Ile Ala Ser Arg Glu Leu Glu Lys Ala Lys
1105                1110                1115                1120

Met Ala Ala Asn Val Ser Ile Thr Gln Pro Glu Ser Thr Gly Glu Pro
                1125                1130                1135

Asn Asn Met Thr Leu Leu Ala Glu Glu Ala Arg Arg Leu Ala Glu Arg
            1140                1145                1150

His Lys Gln Glu Ala Asp Asp Ile Val Arg Val Ala Lys Thr Ala Asn
        1155                1160                1165

Glu Thr Ser Ala Glu Ala Tyr Asn Leu Leu Leu Arg Thr Leu Ala Gly
    1170                1175                1180

Glu Asn Gln Thr Ala Leu Glu Ile Glu Glu Leu Asn Arg Lys Tyr Glu
1185                1190                1195                1200

Gln Ala Lys Asn Ile Ser Gln Asp Leu Glu Lys Gln Ala Ala Arg Val
                1205                1210                1215

His Glu Glu Ala Lys Arg Ala Gly Asp Lys Ala Val Glu Ile Tyr Ala
            1220                1225                1230

Ser Val Ala Gln Leu Thr Pro Val Asp Ser Glu Ala Leu Glu Asn Glu
        1235                1240                1245

Ala Asn Lys Ile Lys Lys Glu Ala Ala Asp Leu Asp Arg Leu Ile Asp
    1250                1255                1260

Gln Lys Leu Lys Asp Tyr Glu Asp Leu Arg Glu Asp Met Arg Gly Lys
1265                1270                1275                1280

Glu His Glu Val Lys Asn Leu Leu Glu Lys Gly Lys Ala Glu Gln Gln
                1285                1290                1295

Thr Ala Asp Gln Leu Leu Ala Arg Ala Asp Ala Ala Lys Ala Leu Ala
            1300                1305                1310

Glu Glu Ala Ala Lys Lys Gly Arg Ser Thr Leu Gln Glu Ala Asn Asp
        1315                1320                1325

Ile Leu Asn Asn Leu Lys Asp Phe Asp Arg Arg Val Asn Asp Asn Lys
    1330                1335                1340

Thr Ala Ala Glu Glu Ala Leu Arg Arg Ile Pro Ala Ile Asn Arg Thr
1345                1350                1355                1360

Ile Ala Glu Ala Asn Glu Lys Thr Arg Glu Ala Gln Leu Ala Leu Gly
                1365                1370                1375

Asn Ala Ala Ala Asp Ala Thr Glu Ala Lys Asn Lys Ala His Glu Ala
            1380                1385                1390

Glu Arg Ile Ala Ser Ala Ala Gln Lys Asn Ala Thr Ser Thr Lys Ala
        1395                1400                1405

Asp Ala Glu Arg Thr Phe Gly Glu Val Thr Asp Leu Asp Asn Glu Val
    1410                1415                1420
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Asn Gly Met Leu Arg Gln Leu Glu Glu Ala Glu Asn Glu Leu Lys Arg
1425                1430                1435                1440

Lys Gln Asp Asp Ala Asp Gln Asp Met Met Met Ala Gly Met Ala Ser
                1445                1450                1455

Gln Ala Ala Gln Glu Ala Glu Leu Asn Ala Arg Lys Ala Lys Asn Ser
            1460                1465                1470

Val Ser Ser Leu Leu Ser Gln Leu Asn Asn Leu Leu Asp Gln Leu Gly
        1475                1480                1485

Gln Leu Asp Thr Val Asp Leu Asn Lys Leu Asn Glu Ile Glu Gly Ser
    1490                1495                1500

Leu Asn Lys Ala Lys Asp Glu Met Lys Ala Ser Asp Leu Asp Arg Lys
1505                1510                1515                1520

Val Ser Asp Leu Glu Ser Glu Ala Arg Lys Gln Glu Ala Ala Ile Met
                1525                1530                1535

Asp Tyr Asn Arg Asp Ile Ala Glu Ile Ile Lys Asp Ile His Asn Leu
            1540                1545                1550

Glu Asp Ile Lys Lys Thr Leu Pro Thr Gly Cys Phe Asn Thr Pro Ser
        1555                1560                1565

Ile Glu Lys Pro
    1570
```

PATENT COOPERATION TREATY

DEC 28 2000

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

To:
McDONNELL BOEHNEN HULBERT
& BERGHOFF
Attn. HARPER, David S.
300 South Wacker Drive
Suite 3200
Chicago, IL 60606
UNITED STATES OF AMERICA

	Date of mailing *(day/month/year)* 27/12/2000
Applicant's or agent's file reference 99,274-D1	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US 00/11543	International filing date *(day/month/year)* 28/04/2000
Applicant BIOSTRATUM, INC. et al.	

1. [X] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Mireille Claudepierre

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